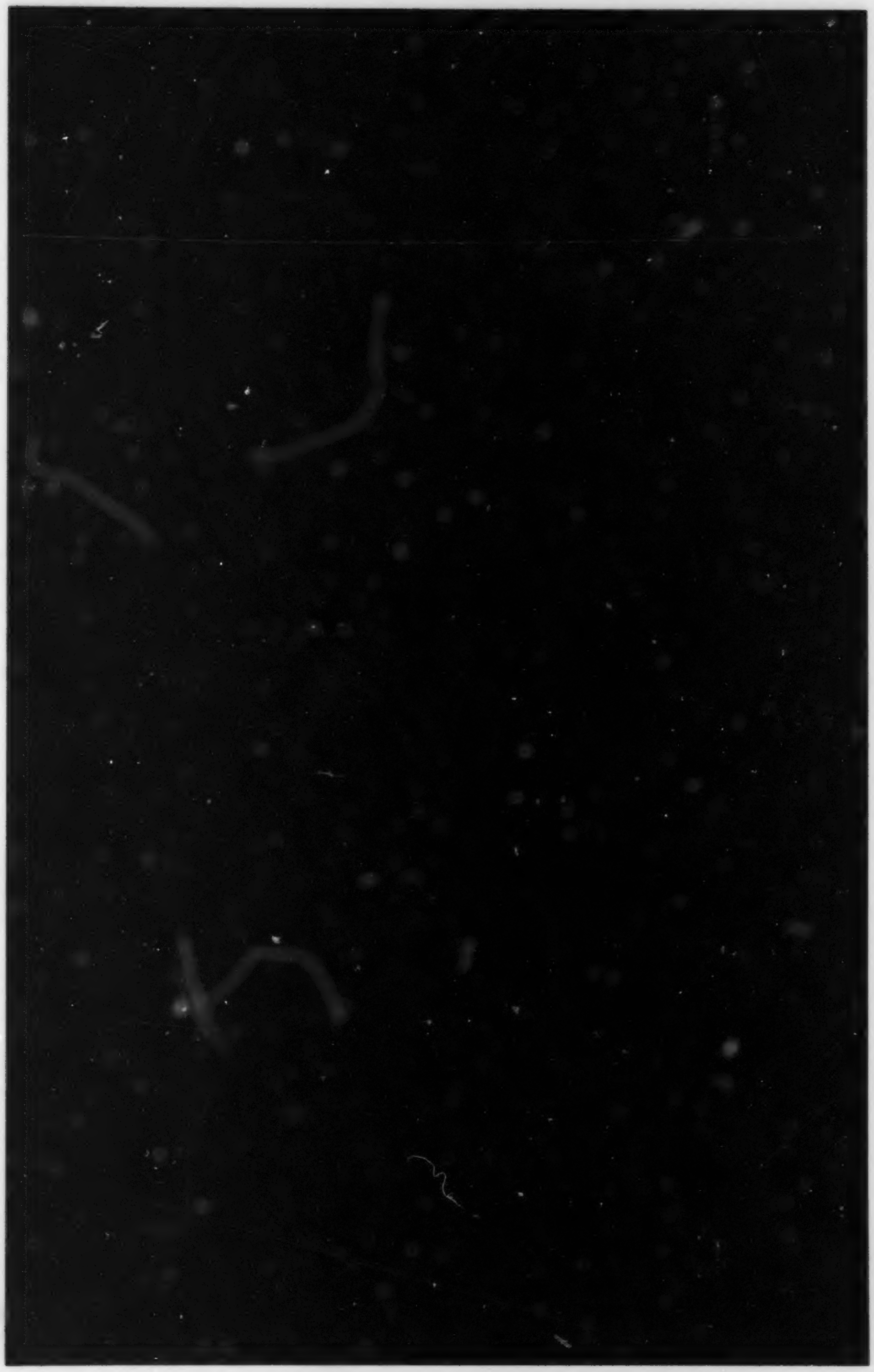

Cancer Control Agency of British Columbia

British Columbia Cancer Research Centre

British Columbia Cancer Foundation

Annual Report 1987-1988

93-00029/

1988 marks the 50th anniversary of cancer treatment in British Columbia. We dedicate this annual report to the pioneers in the medical profession, in nursing and the health delivery system, to the scientists and to an army of volunteers who have helped us achieve the present level of treatment, patient care and research.

William E. Ireland
Chairman

A contribution towards the publication of these annual reports, recognizing the 50th anniversary of cancer treatment in British Columbia, was made by four Canada Safeway employees – Bruce Nicoll, Robyn Blaxland, Bill Micatovich and Jim Spooner. We thank them for their generous support.

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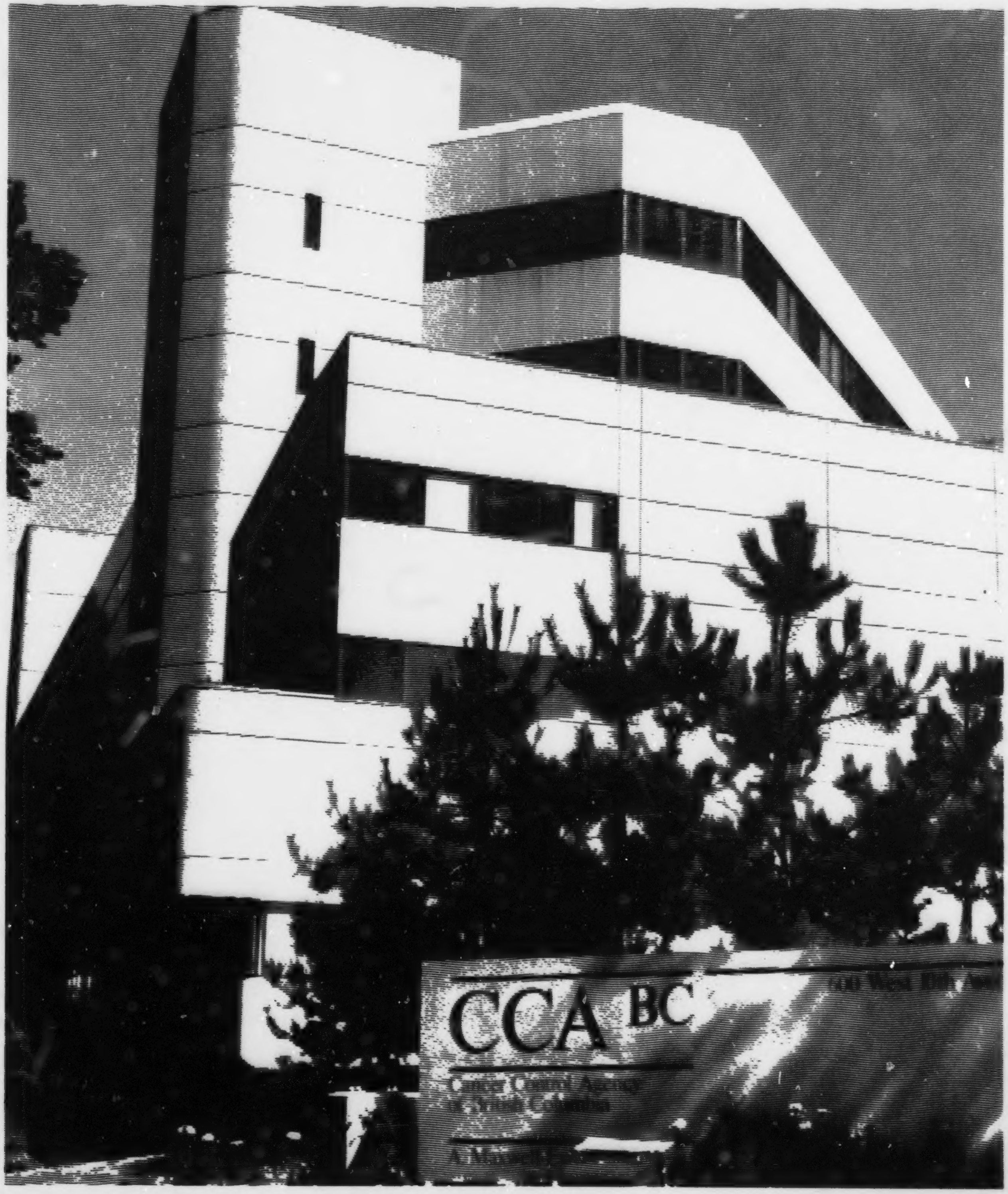
Cover legend: A schematic representation of the way that individual tumour cells are monitored to determine their response to therapy. The treated tumour or 'spheroid' model (top) is stained with a slowly-penetrating fluorescent stain, then reduced to single cells which are processed through a fluorescence-activated cell sorter (FACS Machine) at a rate of several thousand cells per second (middle). Cells with pre-determined amounts of stain are collected (bottom) and assessed for their response to the treatment; the overall fate of the tumour is determined by 'integrating' the individual responses.

Cancer Control Agency of British Columbia


CCA BC
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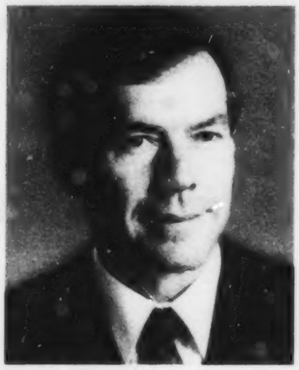
Cancer Control Agency
of British Columbia

Administration



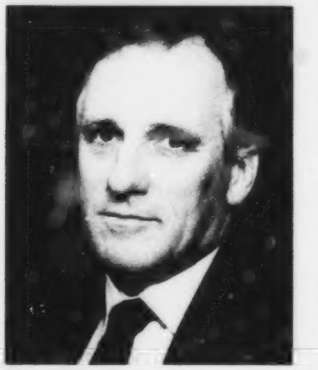
Dr. D.J. Klaassen
Director, CCABC

Mr. R.J. Smith
Deputy Director, CCABC

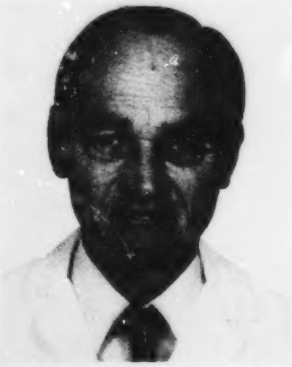
Dr. P. Coy
Director, Victoria Cancer Clinic

Mr. D.C. Richardson
Assistant Deputy Director

Mrs. L.B. Jamieson
Assistant Deputy Director of Nursing and Related Patient Care Services



Mr. P. McAllister
Administrator
Victoria Cancer Clinic



Dr. R.E. Beck
Director, Outreach Program

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Project Building Committee VCC
Gen. B.A. Oxholm

President's Report

Dear Mr. Minister:

On behalf of the Board of Trustees, I am pleased to present the Annual Report of the Cancer Control Agency of British Columbia for the operating year ended March 31, 1988.

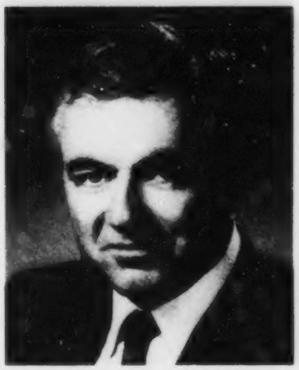
This year we are again combining our Report with those of the British Columbia Cancer Foundation and of the British Columbia Cancer Research Centre to present a more comprehensive overview of the cancer treatment and research currently provided on behalf of the people of British Columbia. We have also included a summary of data compiled by our registry as to the incidence of various cancers within the Province and a comprehensive list of scientific publications documenting many excellent contributions by our professional staff.

The first patients of our new Victoria Cancer Clinic were treated in May. The clinic was opened formally in August by our Honorary Patrons, Their Honours, The Honourable Robert G. Rogers, Lieutenant-Governor of British Columbia and Mrs. Rogers. This facility, equipped to the state of the art, now extends the highest standard of comprehensive cancer care to the residents of Vancouver Island.

The accompanying report of our Director cites our concern that the growing demand for radiotherapy treatment services is outstripping the available facilities of our A. Maxwell Evans Clinic in Vancouver. As short-term responses, we are instituting a second shift in the radiotherapy department and have undertaken the addition of two radiotherapy units within an addition to the clinic building. These are stop-gap measures and the planning of additional cancer treatment facilities within the Province will remain a high priority of our Board in the coming year.

Our Trustees are privileged to serve the people of British Columbia. The Agency is amongst the world leaders in cancer care. It has achieved this recognition through the excellence, interest and commitment of its staff, the leadership of our Board and the support of the medical community at large, of the Ministry of Health and of our volunteers, including the Women's Auxiliary, the IODE and the Order of the Eastern Star. Their contributions are gratefully acknowledged.

William E. Ireland, Q.C.
President and Chairman,
Board of Trustees



William E. Ireland – President

Director's Report

Several important events in the history of the Cancer Control Agency of British Columbia occurred during this past year. As noted in last year's report the former Director, Dr. D. A. Boyes, retired at the beginning of the year after more than thirty years here. The Agency's Deputy Director, Mr. R. J. Smith, left in March 1988 to become the President and C.E.O. of Lions Gate Hospital in North Vancouver. He gave the Agency seven years of outstanding leadership. His successor, Mr. B. Schmidt, will join us from B.C.'s Children's Hospital in July 1988.

In June 1987 the Special Oncology Unit was opened at the A. Maxwell Evans Clinic. This HEPA-filtered isolation ward has allowed us to provide better care for patients receiving autologous bone marrow transplants, biological therapies such as interleukin-2, high dose chemotherapy and intensive radiotherapy treatments. The unit has filled its function well and has allowed us to expand these programs; however, it has placed extra stresses on many of the hospital departments that provide services to it.

The first patients were treated in May 1987 in the newly built Victoria Cancer Clinic on the Royal Jubilee Hospital site in Victoria. The Honourable Robert G. Rogers, Lieutenant-Governor of the Province of B.C., officiated at the opening ceremony in September 1987. This Clinic with its "state-of-the-art" radiotherapy equipment provides the most modern facilities and treatment to the residents of Vancouver Island.

The Agency, with the cooperation and support of the B.C. Cancer Foundation, embarked on a strategic planning program initiated at the annual retreat of the Board and senior management held in May 1987. This important process will not be completed until well into the coming year and will set the stage for our long-range planning. In concert with this process the Agency struck an ad hoc committee to review its computerization needs.

Our primary mandate remains patient care. The staff of the Agency is internationally recognized for the superb multi-disciplinary care that they provide to British Columbians in our treatment facilities and in the Outreach program. However, the pressures that have been placed on radiotherapy treatment services at the A. Maxwell Evans Clinic are giving rise to considerable concern. The provincial government has agreed to allow the Agency to start planning for an urgently needed addition. We hope that we will be allowed to start construction in 1989.

At the Agency we value the relationship we have with other professionals in the province especially the physicians involved with the chemotherapy Outreach and colposcopy programs and consultative clinics. Our cytology laboratory continues to provide an excellent highly utilized service.

Educational activities at all levels, undergraduate, postgraduate, continuing professional and public education, occupy a good portion of the staff's time. We are proud of our accomplishments and participation in this area but hope to expand these in the future.

Our research programs continue to be nationally and internationally recognized for excellence. This is attested to by our staff's publication record, participation in national and international committees, symposia and conferences, and excellent record at obtaining peer-reviewed grants and position funding. Finding the resources to support these programs continues to be a challenge.

Special thanks is extended to our volunteer organizations, the Women's Auxiliary, the Order of the Eastern Star and the IODE. The many hours provided in service to patients, in helping our staff and in fundraising for equipment and projects are gratefully acknowledged. The staff and patients appreciate the support and encouragement of the President, Mr. W. E. Ireland, and the Board of the Agency; they have been particularly helpful in this year of transition in administration.

I would like to thank all concerned for the help and support given to me during my first year at the Agency.

D. J. Klaassen, BA, MD, FRCPC, FACP
Director

Volunteer Organizations

IODE

During 1987 members volunteered approximately 1,500 hours at the Coffee Bar and raised $1,300 in donations which will be used for patients' comforts.

Our Provincial President and I attended the official opening of the Victoria Clinic and we enjoyed a guided tour after the ceremonies. The IODE contributed the furnishings of the main entrance and reception area of the Clinic at a cost of $12,000. A painting by the artist, Jan Crawford, will hang in this area in memory of one of our Victoria members. The painting was contributed by IODE members throughout B.C.

In 1987 it was my privilege to attend the Testimonial Dinner to honour Dr. Boyes on his retirement, the Professional Staff's annual dinner meeting, the CCABC's Board of Trustees annual dinner meeting, the B.C. Cancer Foundation's annual meeting and a tour of the Research Centre during the Foundation's Open House.

This is my final report after sixteen years as Convenor and Chairman of the Jessie R. Burke Fund. I want to take this opportunity to say how much I have enjoyed serving on the Board of Directors of this Foundation as IODE's representative and to thank the staff and administration for their help and support. I hope that our members will continue to provide comfort and service to the patients at the Vancouver and Victoria Clinics.

I want to extend best wishes to my successor, Mrs. Moira Murdoch. May she enjoy the same personal satisfaction which I have experienced.

Nancy Stark,
Chairman, Jessie R. Burke (Memorial) Cancer and Research Fund

ORDER OF THE EASTERN STAR

As Director of Cancer Activities for British Columbia and Yukon Order of the Eastern Star, it is my pleasure to present my report to the Cancer Control Agency of British Columbia.

Our Cancer project is divided into two categories:

1. **Cancer Research**

The Grand Chapter of British Columbia and Yukon Order of the Eastern Star approved the funding for research as follows:

(a)	The Shane Fellowship was given to Dr. Richard Klasa who will serve his fellowship in Advanced Therapeutics in the Special Oncology Unit under Dr. H.K.B. Silver	$18,000
(b)	Physics (Machine Shop) Vertical Milling Machine	22,500
(c)	Victoria Cancer Clinic Balance of committed funds	$16,000
(d)	Erma Boyce Library Funds for books, VCR's, tapes and audio-visuals at the Agency	$2,500
(e)	Special Oncology Unit – 3 small portable TV's with remote controls – 2 VCR's – 2 Chemo treatment chairs – 1 microwave – 1 small refrigerator	5,400
		64,400
2.	**Cancer Dressings**	37,000
	Total	$101,400

A letter from the 1986-87 Shane Fellowship recipient, Dr. I.A. Olivotto, expressed appreciation for the fellowship which enabled him to focus on ways to alter various technical aspects of the surgery and radiation which is offered to patients with early breast cancer in an attempt to define those factors which will optimize the late cosmetic effects of the treatment. Dr. Olivotto returned to full-time practice September 1, 1987.

The Order of the Eastern Star operates over sixty Cancer Dressing Stations in British Columbia and Yukon, where supervisors, convenors and members make and distribute dressings free of charge to cancer patients upon request under medical authority in the respective areas through hospitals and public health nurses. Approximately 99,640 were dispensed from Vancouver Clinic alone.

Our members supply handcrafts of slippers, afghans and stoma bibs and many other commodities to the patients in the Agency, and provide plants at Easter and Christmas for the clinic.

Our sale of cancelled stamps brought over $11,500 this year. Thank you for your continued support. Other means of raising funds are from teas, bazaars and donations.

Dr. David Boyes, who retired as Director of the Agency this past year, will be greatly missed for his encouragement and support of our activities.

It is with regret that Mrs. Arlene Temple's resignation was accepted, for she has given twenty years of dedicated service as Director.

We are grateful for the assistance, advice and many courtesies extended to us by Dr. David Klaassen, Mrs. Bonnie Jamieson, the Board of Trustees and members of the staff of the Cancer Control Agency of British Columbia. My first year in office has been very rewarding.

L. Musgrave
Director of Cancer Activities,
Order of the Eastern Star

Committees of the Cancer Control Agency and Their Chairmen

TUMOUR GROUP COMMITTEES

Bone & Soft Tissue Group
Dr. K.S. Morton

Breast Tumour Group
Dr. V.E. Basco

Central Nervous System Tumour Group
Dr. C.M. Ludgate

Gastro-Intestinal Tumour Group
Dr. W.C. MacDonald

Genito-Urinary Tumour Group
Dr. L.D. Sullivan

Gynecology Tumour Group
Dr. J.L. Benedet

Head & Neck Tumour Group
Dr. A.D. Flores

Lung Tumour Group
Drs. W. Nelems and P. Coy

Lymphoma & Leukemia Tumour Group
Dr. J.M. Connors

Melanoma Tumour Group
Dr. H.K.B. Silver

Ocular & Orbital Tumour Group
Dr. J. Rootman

Pediatric Tumour Group
Dr. C.J.H. Fryer

Skin Tumour Group
Dr. D.I. McLean

MEDICAL/ADMINISTRATIVE COMMITTEES

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Dr. J.H. Goldie

Agency Management Committee
Dr. D.J. Klaassen

AMEC Medical/Dental Staff Association
Dr. S. O'Reilly

Biohazards Committee
Dr. P.S. Rennie

Bone Marrow Transplant Committee
Dr. G.L. Phillips

Cancer Prevention Advisory Commttee
Dr. P.R. Band

Clinical Investigation Committee
Dr. H.K.B. Silver (to Oct. 1/87)
Dr. J.M. Connors

Infection Control Committee
Dr. R.N. Murray

Medical Manpower Committee
Dr. D.J. Klaassen

Medical Records Committee
Dr. C.M.L. Coppin

Nutrition Committee
Dr. W.C. MacDonald

Occupational Health & Safety Committee
L. Svirchev

OR Committee
Dr. R.E. Robins

Palliative Care Committee
Dr. G. McGregor

Patient Care Committee
Dr. J.H. Goldie

Pharmacy & Therapeutics Committee
Dr. I.H. Plenderleith

Professional Advisory Credentials Committee
Dr. G.H. Anderson

Radiation Safety Committee
D.C. Richardson

Research Management Committee
Dr. D.J. Klaassen

Staff Communications Committee
R. Bruce

Symptom Management Committee
Dr. I.H. Plenderleith

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A. Hudson

Ambulatory Care
C. Brown

Chaplaincy
Rev. C. Johnstone

Clinical Laboratory
H. Backlund

Cytology Laboratory
O. Bennett

Data Services
P. Hayles

Diagnostic Imaging
E. Kilby

Distribution Services
D. Sawyer

Employee Relations
R. Bruce

Finance
D. Morrison

Hospital 5 West
H. Mielcarski

Hospital 5 East
B. Hiltz

Hospital 6 West
P. Azad

Hospital 6 East
B. McDermott

Library
D. Noble

Medical Illustration
S. Robertson

Medical Records
L. Christian

Mould Room
R. Allen

Nutrition
M. Baker

Plant Operations
V. Lynnerup

Prosthetics
H. Drake

Purchasing
J. Easton

Radiotherapy
G. Sherstan

CCABC Professional Staff

MEDICAL, DENTAL AND SCIENTIFIC STAFF

DIRECTOR

D.J. Klaassen, BA,MD,FRCPC, FACP
Clinical Professor (Medicine)

CLINICAL HEMATOLOGY

A.C. Eaves, BSc,MSc,MD, PhD, FRCPC,FACP
Head
Professor (Medicine and Pathology)

M. Barnett, BMedSci,MD,BS, MRCP
Clinical Assistant Professor (Medicine)

D.E. Hogge, BScMed,MD, PhD,FRCPC
Clinical Assistant Professor (Medicine)

R.K. Humphries, BSc,MSc,MD, PhD
Assistant Professor (Medicine)

H-G. Klingemann, MD
Clinical Associate Professor (Medicine)

P.M. Lansdorp, MD,PhD
Clinical Assistant Professor (Medicine)

G.L. Phillips, MD,ABIM
Associate Professor (Medicine)

D. Reece, MD,ABIM,FRCPC
Clinical Assistant Professor (Medicine)

J. Shepherd, MD,FRCPC
Clinical Instructor

J. Moquin, MD
BMT Fellow

N. Graham, MD
Clinical Associate

M. Jancewicz, MD
Clinical Associate

J. Brandwein, MD
Hematology Resident

M. Harakati, MD
Hematology Resident

L. Puil, MD
Hematology Resident

TERRY FOX LABORATORY

A.C. Eaves*
Head

C.J. Eaves, BA,MSc,Phd
Professor (Medical Genetics)

D.E. Hogge*

R.K. Humphries*

D.K. Kalousek, MD, FRCPC, FCCMG
Associate Professor (Pathology)

G. Krystal, BSc,MSc,PhD
Associate Professor (Pathology)

P.M. Lansdorp*

D.L. Mager, BSc,MSc,PhD
Associate Professor (Medical Genetics)

F. Takei, BSc,PhD
Associate Professor (Pathology)

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A.J. Worth, MD,FRCPC
Head
Clinical Professor (Pathology)

D.E. Horsman, MD,FRCPC
Clinical Assistant Professor (Pathology)

K.G. Lerner, MD,FACP
Clinical Assistant Professor (Pathology)

A. Millner, MD,FRCPC
Clinical Instructor (Pathology)

F.J. Roberts, MD,FRCPC
Clinical Professor (Pathology)

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Clinical Professor (Pathology)

J.C. LeRiche, MB,ChB,FRCPC
Clinical Associate Professor (Pathology)

J.P. Matisic, MD,FRCPC
Clinical Instructor (Pathology)

K.C. Suen, MD,FRCPC
Clinical Professor (Pathology)

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P. Stevenson-Moore, BDS, LDSRCS,MSD,MRCDC
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Honorary Assistant Professor (Dentistry)

J.B. Epstein, DMD,MSD
Clinical Assistant Professor (Dentistry)

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Head
Associate Professor (Medicine)

A. Lam, MD,FRCPC
Clinical Instructor (Medicine)

L.M. Warshawski, MD,FRCPC
Clinical Instructor (Medicine)

DIAGNOSTIC IMAGING

H.A. Mueller, BA,MD,DABR, FACR
Head
Clinical Professor (Diag Rad)

S.M. Bhimji, MD,ChB,FRCPC
Clinical Assistant Professor (Diag Rad)

D. Harrison, BSc,MD,FRCPC
Clinical Assistant Professor (Diag Rad)

J. Morgan-Parkes, MD,FRCPC
Clinical Associate Professor (Diag Rad)

P.Hassell, BSc,MDCM,FRCPC

EPIDEMIOLOGY, BIOMETRY AND OCCUPATIONAL ONCOLOGY

P.R. Band. BA,MD,FRCPC
Head
Honorary Professor (Medicine)
Clinical Professor (Health Care & Epi)

A.J. Coldman, BSc,MA, Diploma in Epidemiology, PhD

R.P. Gallagher, BSc,MA
Clinical Assistant Professor (Health Care & Epi)
Associate Member (Ophthalmology)

T.G. Hislop, BSc,MSc,MD,CM
Clinical Assistant Professor (Health Care & Epi)

M.L. McBride, BA,MSc
Honorary Lecturer (Health Care & Epi)

---

*Academic credentials and clinical appointments noted elsewhere.

J.J. Spinelli, BSc,MSc
Honorary Lecturer (Health Care & Epi)
W.J. Threlfall, BSc,MSc
V.T.Y. Ng, MMath

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P.J. Hoskins*
M.F. Manji*
E. Martin, MD
Clinical Associate
E.J. McMurtrie, MD,FRCSC
Clinical Instructor (Obs & Gyne)
J. Pike, MD
Clinical Associate
K.D. Swenerton*
M. Turko, MD,FRCSC
Associate Professor (Obs & Gyne)
F.L.W. Wong*
J. Blake, MD
(Resident)
L. Elit, MD
(Resident)
K. Jaroudi, MD
(Resident)
D. Millar, MD
(Resident)

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Clinical Associate Professor (Medicine)
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(Interior Clinic)
K. Gelmon, BA,MD,FRCPC
Clinical Assistant Professor (Medicine)
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Clinical Assistant Professor (Medicine)
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M.A. Knowling, MD,FRCPC
Clinical Assistant Professor (Medicine)
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Associate Professor (Medicine)
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Clinical Associate Professor (Medicine)
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Clinical Professor (Medicine)
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Clinical Professor (Medicine)
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Clinical Associate Professor (Medicine)
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Clinical Assistant Professor (Medicine)
H.K.B. Silver*
D.S. Stuart, MD,FRCPC
Clinical Instructor (Medicine)
K.D. Swenerton, MD,FRCPC
Clinical Associate Professor (Medicine)
K.S. Wilson, MB,FRCP(Edin), FRCPC,FACP
(Victoria)
Clinical Assistant Professor (Medicine)
A. Al-Faraj, MB,BCh,ArBIM
(Resident)
J. Atiba, MBBS
(Resident)
C. Bryce, MD
(Resident)
M. McLaughlin, MD,FRCP, ABIM
(Resident)
B. Lesperance, MD,FRCP, ABIM
(Resident)

SECTION OF ADVANCED THERAPEUTICS

H.K.B. Silver, BSc,MD,PhD, FRCPC,FACP
Head
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F.A. Salinas, BS,DVM
Clinical Professor (Pathology)
S.R. Dedhar, BSc,MSc,PhD
Assistant Professor (Pathology)
R.J. Klasa, MD CM,FRCPC

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Professor Emeritus (Biochemistry)
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P.W. Gout, PhD
E.C. Jones, MD,FRCPC
R.L. Noble, MD,PhD,DSc (London),FRSC
Professor Emeritus (Physiology)
Honorary Member, CCABC Professional Staff
P.S. Rennie, PhD
Honorary Professor (Surgery)

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Associate Professor (P.T.)(Ped)

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P. Rogers, MB,MRCP(UK), FRCPC
Associate Professor (Ped)

J.M. Teasdale, MB,ChB,FRCPC
Associate Professor (Ped)

RADIATION ONCOLOGY

S.M. Jackson, MB,ChB,MD (Manchester), DMRT,FRCR,FRCPC
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Clinical Professor (Surgery)

B.D. Acker, BSc(Hon),MD, DABR,FRCPC
Clinical Assistant Professor (Surgery)

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M. Chu, MD,CCFP

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J.L. Matheson, MD

M.F. Manji, MB,ChB,DMRT, MD,DABR,FRCPC
Clinical Assistant Professor (Surgery)

I.A. Olivotto, MD,FRCPC
Clinical Instructor (Surgery)

N.J.S. Voss, LRCP,MRCS,DMRT, FRCR,FRCPC
Clinical Assistant Professor (Surgery)

F.L-W. Wong, BSc(Hon. Biochem),MD,FRCPC
Clinical Instructor

A. Agranovich, MD
(Resident)

G. Jones, BSc,(Hon. Biochem & Chem),MD
(Resident)

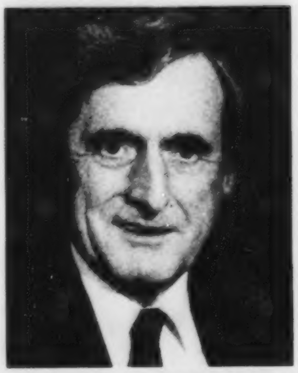
M. Mildenberger, BSc,MD
(Resident)

G. Okawara, M.Eng,MBA,MD
(Resident)

M.M. McKenzie, BSc,MD
(Resident)

W.J. Morris, BSc,MSc,MD
(Resident)

SECTION OF DEVELOPMENTAL RADIOTHERAPY



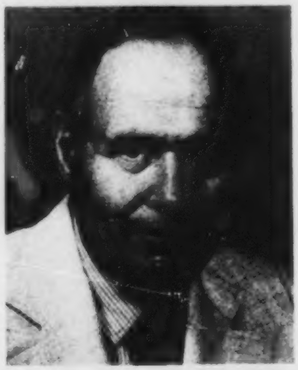
G.B. Goodman, FRCPC,FRCP (Edin),FRCR,FACR
Head
Clinical Professor (Surgery)

B.D. Acker*

D.E. Rheaume, MD,FRCPC(Int Med),FRCPC(Rad Onc)
Clinical Fellow – TRIUMF

H. Shirato, MD
Clinical Fellow – TRIUMF

RADIATION PHYSICS



R.O. Kornelsen, BSc,MSc,PhD, FCCPM
Head
Honorary Lecturer

R.W. Harrison, BSc,MSc

S.G. Hussein, BSc,MSc,PhD, FCCPM

G.M. Kennelly, BSc,FCCPM

W.S.Y. Kwa, BSc,MSc,MCCPM

K.Y. Lam, BSc,PhD
Honorary Assistant Professor

D.M. Linekin, BSc,MSc,PhD
(Victoria)

B. McParland, BSc,MSc,PhD, MCCPM
(Victoria)

L.J. Watts, BSc,MSc

K.F.K. Yuen, BSc,MSc,PhD

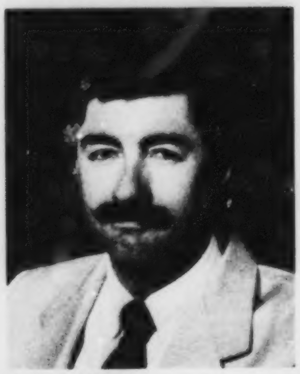
SURGICAL ONCOLOGY

R.E. Robins, MD,FRCSC
Head
Clinical Professor (Surgery)

SENIOR ALLIED PROFESSIONAL STAFF

M. Baker, BSc (Hon.Dietetics)

L. Chow, BSc(Pharm)



R. Doll, MSW
Field Instructor (Social Work)

Rev. C. Johnstone, BA,BD, ThM
Adjunct Faculty
(Vancouver School of Theology)

D. Noble, BSc,BLS

D.C. Richardson, B.Comm, CCHSE(C)

L.B. Jamieson, RN,BScN,MBA

R.J. Smith, B.Comm,MBA, CCHSE(C)
Honorary Lecturer (Health Care & Epi)

Five-Year Financial Highlights

Expenditures

The increase in total expenditures over the past five years shows the growing role of the Agency in assuming financial responsibility for cancer care in the province.

	1987/88 **$ 000**	1986/87 $ 000	1985/86 $ 000	1984/85 $ 000	1983/84 $ 000
Operating Fund	**$55,199**	$50,303	$45,156	$37,921	$32,400
Investigative Grants Fund	**3,134**	2,914	2,206	2,222	1,799
Plant Fund	**1,345**	6,508	2,705	7,913	14,480
Total Expenditures	**$59,678**	$59,725	$50,067	$48,056	$48,679

Net Operating Results

The deficits for the current and immediately preceding years were incurred as planned to utilize the accumulated surplus from previous years.

Excess (Deficiency) of Operating Fund revenue over expenditure for the year	**$ (571)**	$ (1,180)	$ (1,274)	$ 1,357	$ 1,013
% of Operating Fund expenditure	**(1.0%)**	(2.3%)	(2.8%)	3.6%	3.1%

Financial Statements

Condensed Statements of Revenue, Expenditure and Surplus

For the year ended March 31, 1988
with comparative figures for the
year ended March 31, 1987

		1988 **$ 000**	1987 $ 000
Operating Fund			
Revenue	Government grants	**$51,913**	$45,275
	Recoveries for services	**1,737**	2,800
	Investment and other income	**978**	1,048
		54,628	49,123
Expenditure	Salaries, wages and benefits	**37,496**	34,782
	Patient care	**11,781**	10,463
	Plant and support services	**5,922**	5,058
		55,199	50,303
Current year's excess (deficiency) of revenue over expenditure		**(571)**	(1,180)
Surplus, beginning of year		**1,011**	2,191
Surplus, end of year		**$ 440**	$ 1,011
Plant Fund			
Surplus, beginning of year		**$45,099**	$41,226
Add:	Capital grants received	**1,273**	6,526
		46,372	47,752
Deduct: Depreciation		**(3,086)**	(2,653)
Surplus, end of year		**$43,286**	$45,099

The information shown in the condensed financial statements is extracted from the Agency's full financial statements for the year ended March 31, 1988 on which the Agency's auditors, Clarkson Gordon, have reported. Copies of their report and of the full financial statements are available on request.

Financial Statements

Condensed Balance Sheets

as at March 31, 1988
with comparative figures as at
March 31, 1987

		1988 $ 000	1987 $ 000
Operating Fund			
Assets	Cash	**$ 3,128**	$ 3,525
	Amounts receivable	**1,926**	2,823
	Inventory of supplies & prepaid expenses	**988**	1,063
		$ 6,042	$ 7,411
Liabilities and Surplus	Accounts payable and accruals	**$ 3,843**	$ 6,400
	Deferred income	**1,759**	–
	Surplus	**440**	1,011
		$ 6,042	$ 7,411
Plant Fund			
Assets	Buildings and equipment	**$43,286**	$40,487
	Construction in progress	**–**	4,612
		$43,286	$45,099
Surplus		**$43,286**	$45,099

The information shown in the condensed financial statements is extracted from the Agency's full financial statements for the year ended March 31, 1988 on which the Agency's auditors, Clarkson Gordon, have reported. Copies of their report and of the full financial statements are available on request.

CCABC Patient Statistics

	April 87 – March 88			April 86 – March 87		
	Vancouver Clinic	Victoria Clinic	Outreach Clinics	Vancouver Clinic	Victoria Clinic	Outreach Clinics
New Patient examinations (including second sites)	5,892	1,319	782	5,516	1,314	850
Treatments: Radiation						
Patients completed – All modalities	5,323	1,257	–	5,211	1,318	–
Fields treated						
X-rays and cobalt	130,113	33,413	–	122,456	28,141	–
Radium and caesium	548	76	–	341	50	–
Other	–	–	–	1	–	–
Total	130,661	33,489	–	122,798	28,191	–
Patient visits	60,496	14,879	–	58,514	12,271	–
Treatments: Chemotherapy						
Patients started	6,060	N/A	–	5,691	N/A	–
Patient visits	10,113	1,328	–	9,666	970	–
Other Ambulatory Care Visits	34,112	8,791	5,641	33,943	9,412	5,768

N/A Not Available

Number of Referred Cases to the Vancouver and Victoria Cancer Clinics

January — December 1987

Site/Histology	Vancouver	Victoria
BREAST	1,047	289
ENDOCRINE GLANDS		
Thyroid Gland	44	8
Other Endocrine Glands	8	2
GASTROINTESTINAL		
Colon	206	65
Esophagus	80	13
Gallbladder & Biliary Tract	23	2
Liver	20	0
Pancreas	68	12
Rectum, Rectosigmoid & Anus	245	48
Small Intestine	7	1
Stomach	92	13
GENITOURINARY		
Kidney, Ureter, Urethra	85	13
Penis & Other Male Genital Organs	2	2
Prostate	641	134
Testicle	69	7
Urinary Bladder	147	19
GYNECOLOGY		
Cervix Uteri	116	18
Corpus Uteri (Endometrium, Myometrium)	252	47
Ovary, Fallopian Tube & Broad Ligament	157	42
Placenta (Hydatidiform Mole)	7	0
Other & Unspecified Female Genital Organs	30	1

Site/Histology	Vancouver	Victoria
HEAD & NECK		
Eye & Lacrimal Gland	6	0
Larynx	110	24
Lip	15	1
Mouth	90	19
Nasal Cavities	21	4
Pharynx	99	26
Salivary Glands	9	4
LUNG, THYMUS, HEART & MEDIASTINUM		
Trachea, Bronchus & Lung	877	244
Thymus, Heart & Mediastinum	11	2
PRIMARY UNKNOWN	145	42
RETROPERITONEUM	5	1
SKIN	409	110
CENTRAL NERVOUS SYSTEM		
Brain	132	28
Other & Unspecified Parts of the Nervous System	13	0
MALIGNANT MELANOMA	275	52
MESOTHELIOMAS	15	4
RETICULOENDOTHELIAL & HEMATOPOIETIC SYSTEMS		
Hodgkin's Disease	68	10
Leukemia	96	15
Multiple Myeloma	56	20
Non-Hodgkin's Disease	261	61
Other Malignant & Borderline Diseases of the Reticuloendothelial & Hematopoietic Systems	24	2
SARCOMA		
Bones, Joints, Articular Cartilage, Connective Subcutaneous & Soft Tissue	86	8
Kaposi's Sarcoma	29	0
NON-CANCER	175	31
MISCELLANEOUS	5	1
TOTALS	6,378	1,445
YOUTH CANCERS (included in above breakdown)	112	6

Ten Most Frequent Types of Cancer

(by Sex and Age Group)

Referred to the Vancouver Cancer Clinic in 1987

	0-16		17-24		25-34		35-44		45-54		55-64		65-74		75-84		85+		TOTAL		GRAND TOTAL
	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	
Breast	0	0	1	0	32	0	148	0	221	1	260	3	253	3	96	1	28	0	1039	8	1047
Trachea, Bronchus, Lung	0	0	0	0	0	3	11	14	46	62	83	181	125	219	30	90	5	8	300	577	877
Prostate	—	0	—	0	—	0	—	3	—	11	—	121	—	341	—	154	—	11	—	641	641
Skin	1	3	0	0	6	6	7	7	17	30	31	48	62	59	43	55	21	13	188	221	409
Malignant Melanoma	0	0	6	0	23	16	33	21	26	35	25	25	22	28	9	6	0	0	144	131	275
Non-Hodgkin's Lymphoma	0	5	3	5	4	9	8	18	16	19	24	31	31	41	13	21	8	5	107	154	261
Corpus Uteri	0	—	0	—	4	—	8	—	40	—	70	—	91	—	37	—	2	—	252	—	252
Rectum, Rectosigmoid, & Anus	0	0	0	0	0	0	4	5	17	15	29	48	31	46	17	26	4	3	102	143	245
Colon	0	0	1	0	1	1	6	7	13	7	28	35	36	35	22	13	0	1	107	99	206
Ovary, Fallopian Tube, Broad Ligament	0	—	4	—	6	—	20	—	43	—	39	—	37	—	7	—	1	—	157	—	157

Ten Most Frequent Types of Cancer

(by Sex and Age Group)

Referred to the Victoria Cancer Clinic in 1987

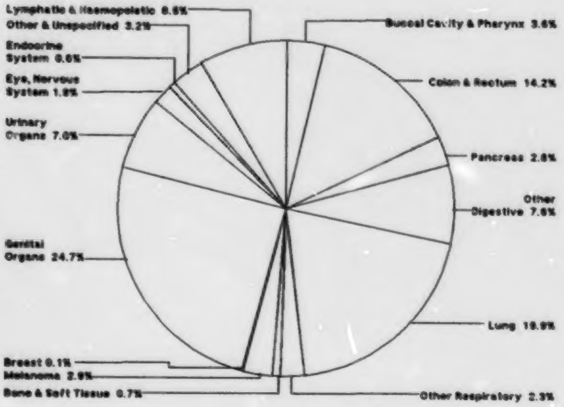
	0-16		17-24		25-34		35-44		45-54		55-64		65-74		75-84		85+		TOTAL		GRAND TOTAL
	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	
Breast	0	0	0	0	6	0	25	0	29	0	92	1	96	0	36	0	4	0	288	1	289
Trachea, Bronchus, Lung	0	0	0	0	0	0	2	3	12	12	27	32	31	76	13	29	2	5	87	157	244
Prostate	—	0	—	0	—	0	—	0	—	6	—	28	—	69	—	29	—	2	—	134	134
Skin	0	0	0	0	1	0	0	2	3	3	3	13	15	22	14	19	7	8	43	67	110
Colon	0	0	0	0	0	0	0	1	1	2	8	18	12	12	4	7	0	0	25	40	65
Non-Hodgkin's Lymphoma	1	2	1	2	0	1	1	5	5	1	1	8	9	9	9	6	0	0	27	34	61
Malignant Melanoma	0	0	1	0	3	2	6	6	7	3	8	2	2	8	2	1	1	0	30	22	52
Rectum, Rectosigmoid, & Anus	0	0	0	0	1	0	1	1	0	3	8	7	7	11	4	4	1	0	22	26	48
Corpus Uteri	0	—	0	—	0	—	2	—	5	—	9	—	19	—	10	—	2	—	47	—	47
Ovary, Fallopian Tube, Broad Ligament	0	—	1	—	0	—	4	—	6	—	15	—	9	—	5	—	2	—	42	—	42
Primary Unknown	0	0	0	0	2	0	1	0	6	2	8	6	3	8	1	3	0	2	21	21	42

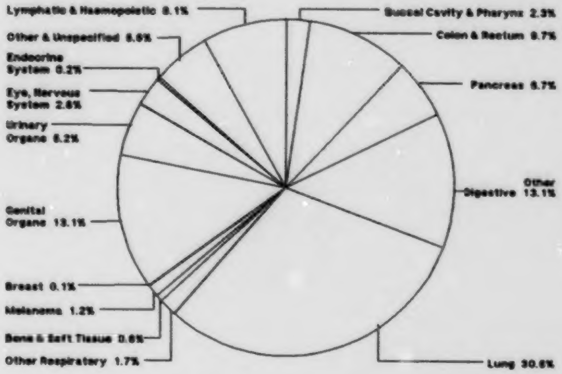
B.C. Cancer Statistics 1986

Relative Frequency of New Cases of Cancer Diagnosed in 1986

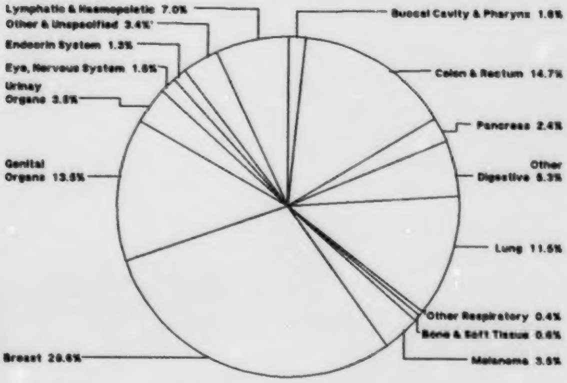
Relative Frequency of Cancer Deaths in 1986

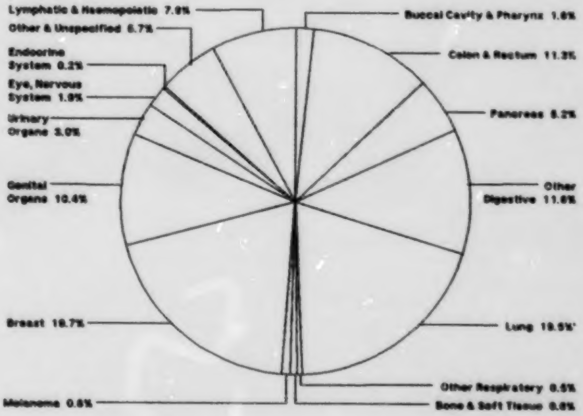
Males
15 and
over



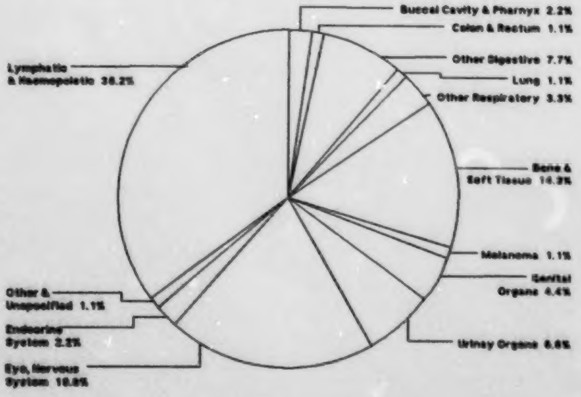


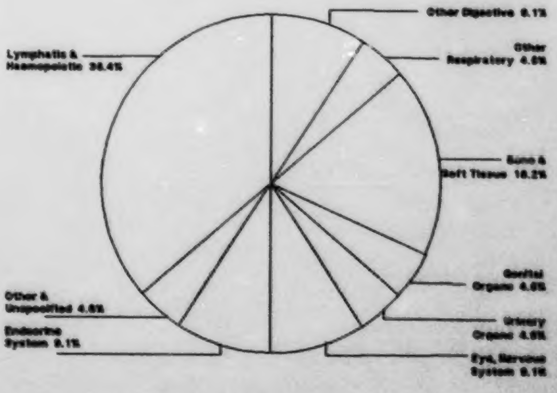
Females
15 and
over



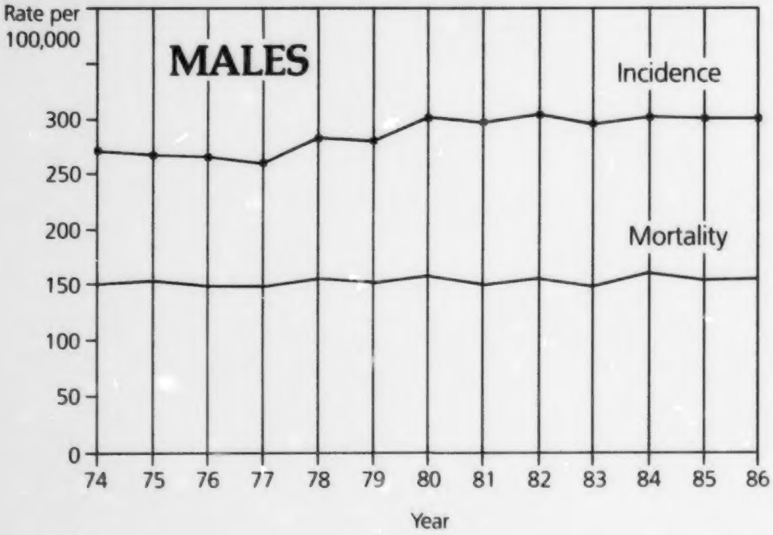


Children
under 15

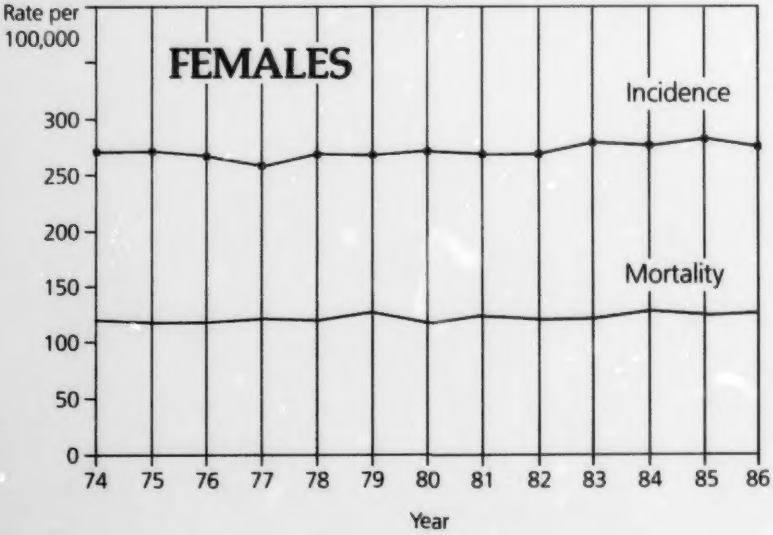




Age-Standardized Incidence and Mortality Rates For All Cancers Diagnosed in B.C., 1974 - 1986 (Invasive cases only; excludes basal and squamous cell cancers of skin)



Age-Standardized Incidence and Mortality Rates For All Cancers Diagnosed in B.C., 1974 - 1986 (Invasive cases oniy; excludes basal and squamous cell cancers of skin)



New Cancer Primaries by Sex and Age-Group

	0 - 34		35 - 44		45 - 54		55 - 64		65 - 74		75 - 84		85 - UP		TOTAL	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Lip	0	0	0	0	6	2	10	1	20	1	12	3	1	0	49	7
Tongue	2	0	4	1	3	0	10	5	10	7	4	5	0	3	33	21
Mouth	2	2	7	1	10	1	10	10	15	9	6	6	1	1	51	30
Pharynx	0	2	10	3	11	8	25	5	22	6	6	1	2	0	76	25
Esophagus	0	0	1	0	6	1	22	5	33	15	19	5	7	7	88	33
Stomach	1	0	3	2	22	14	40	10	58	26	57	47	19	17	200	116
Small Intestine	1	0	0	0	2	4	5	2	12	0	2	4	0	1	22	11
Colon	3	1	10	11	39	29	87	92	165	140	131	156	35	72	470	501
Rectum	0	8	11	6	23	26	90	40	128	83	80	61	11	40	343	264
Liver	5	2	4	1	5	3	21	6	16	6	17	10	7	6	75	34
Gallbladder	0	0	1	0	1	4	11	8	17	16	6	16	1	11	37	55
Pancreas	2	0	1	7	9	6	41	24	53	40	38	31	14	16	158	124
Larynx	0	0	1	0	16	3	32	1	26	2	14	0	2	0	91	6
Trachea, Bronchus, Lung	2	5	17	15	91	61	260	161	420	218	299	107	44	33	1133	600
Bone, Connective Tissue	13	13	5	7	7	0	7	4	7	6	9	6	1	2	49	38
Melanoma-Skin	26	43	29	37	24	25	35	27	34	31	13	15	3	6	164	184
Other Skin	71	53	169	168	279	233	583	392	849	570	523	423	140	193	2614	2032
Breast	0	39	0	162	1	233	2	380	1	404	2	222	0	97	6	1537
Cervix	0	27	0	30	0	19	0	25	0	16	0	8	0	2	0	127
Uterus	0	2	0	14	0	28	0	93	0	118	0	49	0	8	0	312
Ovary	0	10	0	16	0	36	0	64	0	55	0	31	0	8	0	220
Other Female Genital Organs	0	3	0	2	0	3	0	4	0	6	0	17	0	9	0	44
Prostate	0	0	3	0	21	0	205	0	546	0	412	0	140	0	1327	0
Testis	49	0	11	0	8	0	3	0	1	0	0	0	0	0	72	0
Bladder	2	2	9	2	15	4	62	14	82	34	65	22	23	15	258	93
Kidney	5	5	3	5	17	10	44	18	47	28	24	22	4	5	144	93
Brain	17	17	7	2	13	8	22	15	29	18	9	7	1	1	98	68
Thyroid	3	18	4	13	7	19	5	7	6	5	4	3	0	1	29	66
Non-Hodgkin's Lymphoma	19	8	21	12	25	14	50	24	65	52	36	37	8	11	224	158
Hodgkin's Disease	21	17	5	4	4	4	3	4	3	4	1	1	0	1	37	35
Multiple Myeloma	0	0	1	2	9	3	7	7	22	15	24	16	5	8	68	51
Leukemia: Acute Lymphatic	18	12	2	0	0	0	0	1	0	0	2	0	2	2	24	15
Chronic Lymphatic	1	0	0	2	10	3	24	12	16	10	12	9	5	8	68	44
Acute Granulocytic	1	4	3	0	6	2	4	4	3	0	2	3	1	4	20	17
Chronic Granulocytic	3	3	4	1	2	1	7	3	8	3	5	4	0	1	29	16
Other & Unspecified	4	2	2	2	5	2	4	4	11	7	7	14	1	5	34	36
Other Primary Sites	14	12	6	1	12	9	19	10	20	14	21	13	6	14	98	73
Unknown & Ill-Defined Sites	1	1	8	5	15	12	34	33	52	60	61	38	10	31	181	180
TOTAL	286	311	362	534	724	830	1784	1515	2797	2025	1923	1412	494	639	8370	7266

B.C. Cancer Statistics 1986

Incidence Rates (per 100,000) by Sex and Age-Group

	0 - 34		35 - 44		45 - 54		55 - 64		65 - 74		75 - 84		85 - UP		TOTAL	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Lip	0.0	0.0	0.0	0.0	4.0	1.4	7.4	0.7	20.5	0.8	27.2	5.0	10.5	0.0	3.4	0.5
Tongue	0.3	0.0	1.8	0.5	2.0	0.0	7.4	3.5	10.2	5.9	9.1	8.3	0.0	14.8	2.3	1.4
Mouth	0.3	0.3	3.2	0.5	6.6	0.7	7.4	7.1	15.4	7.6	13.6	10.0	10.5	4.9	3.6	2.1
Pharynx	0.0	0.3	4.6	1.4	7.3	5.6	18.5	3.5	22.5	5.1	13.6	1.7	21.1	0.0	5.3	1.7
Esophagus	0.0	0.0	0.5	0.0	4.0	0.7	16.3	3.5	33.8	12.7	43.1	8.3	73.7	34.5	6.1	2.3
Stomach	0.1	0.0	1.4	0.9	14.6	9.8	29.6	7.1	59.4	22.0	129.3	77.9	200.0	83.7	14.0	8.0
Small Intestine	0.1	0.0	0.0	0.0	1.3	2.8	3.7	1.4	12.3	0.0	4.5	6.6	0.0	4.9	1.5	0.8
Colon	0.4	0.1	4.6	5.2	25.9	20.2	64.4	65.1	169.1	118.4	297.1	258.7	368.4	354.7	32.8	34.4
Rectum	0.0	1.1	5.1	2.8	15.3	18.1	66.7	28.3	131.1	70.2	181.4	101.2	115.8	197.0	24.0	18.1
Liver	0.6	0.3	1.8	0.5	3.3	2.1	15.6	4.2	16.4	5.1	38.5	16.6	73.7	29.6	5.2	2.3
Gallbladder	0.0	0.0	0.5	0.0	0.7	2.8	8.1	5.7	17.4	13.5	13.6	26.5	10.5	54.2	2.6	3.8
Pancreas	0.3	0.0	0.5	3.3	6.0	4.2	30.4	17.0	54.3	33.8	86.2	51.4	147.4	78.8	11.0	8.5
Larynx	0.0	0.0	0.5	0.0	10.6	2.1	23.7	0.7	26.6	1.7	31.7	0.0	21.1	0.0	6.4	0.4
Trachea, Bronchus, Lung	0.3	0.7	7.8	7.1	60.5	42.6	192.6	113.9	430.3	184.4	678.0	177.4	463.2	162.6	79.2	41.2
Bone, Connective Tissue	1.7	1.7	2.3	3.3	4.7	0.0	5.2	2.8	7.2	5.1	20.4	10.0	10.5	9.9	3.4	2.6
Melanoma-Skin	3.3	5.6	13.4	17.4	16.0	17.4	25.9	19.1	34.8	26.2	29.5	24.9	31.6	29.6	11.5	12.6
Other Skin	9.1	7.0	77.8	79.0	185.5	162.6	431.9	277.2	869.9	482.2	1185.9	701.5	1473.7	950.7	182.7	139.4
Breast	0.0	5.1	0.0	76.2	0.7	162.6	1.5	268.7	1.0	341.8	4.5	368.2	0.0	477.8	0.4	105.4
Cervix	0.0	3.5	0.0	14.1	0.0	13.3	0.0	17.7	0.0	13.5	0.0	13.3	0.0	9.9	0.0	8.7
Uterus	0.0	0.3	0.0	6.6	0.0	19.5	0.0	65.8	0.0	99.8	0.0	81.3	0.0	39.4	0.0	21.4
Ovary	0.0	1.3	0.0	7.5	0.0	25.1	0.0	45.3	0.0	46.5	0.0	51.4	0.0	39.4	0.0	15.1
Other Female Genital Organs	0.0	0.4	0.0	0.9	0.0	2.1	0.0	2.8	0.0	5.1	0.0	28.2	0.0	44.3	0.0	3.0
Prostate	0.0	0.0	1.4	0.0	14.0	0.0	151.9	0.0	559.4	0.0	934.2	0.0	1473.7	0.0	92.7	0.0
Testis	6.3	0.0	5.1	0.0	5.3	0.0	2.2	0.0	1.0	0.0	0.0	0.0	0.0	0.0	5.0	0.0
Bladder	0.3	0.3	4.1	0.9	10.0	2.8	45.9	9.9	84.0	28.8	147.4	36.5	242.1	73.9	18.0	6.4
Kidney	0.6	0.7	1.4	2.4	11.3	7.0	32.6	12.7	48.2	23.7	54.4	36.5	42.1	24.6	10.1	6.4
Brain	2.2	2.2	3.2	0.9	8.6	5.6	16.3	10.6	29.7	15.2	20.4	11.6	10.5	4.9	6.8	4.7
Thyroid	0.4	2.4	1.8	6.1	4.7	13.3	3.7	5.0	6.1	4.2	9.1	5.0	0.0	4.9	2.0	4.5
Non-Hodgkin's Lymphoma	2.4	1.1	9.7	5.6	16.6	9.8	37.0	17.0	66.6	44.0	81.6	61.4	84.2	54.2	15.7	10.8
Hodgkin's Disease	2.7	2.2	2.3	1.9	2.7	2.8	2.2	2.8	3.1	3.4	2.3	1.7	0.0	4.9	2.6	2.4
Multiple Myeloma	0.0	0.0	0.5	0.9	6.0	2.1	5.2	5.0	22.5	12.7	54.4	26.5	52.6	39.4	4.8	3.5
Leukemia: Acute Lymphatic	2.3	1.6	0.9	0.0	0.0	0.0	0.0	0.7	0.0	0.0	4.5	0.0	21.1	9.9	1.7	1.0
Chronic Lymphatic	0.1	0.0	0.0	0.9	6.6	2.1	17.8	8.5	16.4	8.5	27.2	14.9	52.6	39.4	4.8	3.0
Acute Granulocytic	0.1	0.5	1.4	0.0	4.0	1.4	3.0	2.8	3.1	0.0	4.5	5.0	10.5	19.7	1.4	1.2
Chronic Granulocytic	0.4	0.4	1.8	0.5	1.3	0.7	5.2	2.1	8.2	2.5	11.3	6.6	0.0	4.9	2.0	1.1
Other & Unspecified	0.5	0.3	0.9	0.9	3.3	1.4	3.0	2.8	11.3	5.9	15.9	23.2	10.5	24.6	2.4	2.5
Other Primary Sites	1.8	1.6	2.8	0.5	8.0	6.3	14.1	7.1	20.5	11.8	47.6	21.6	63.2	69.0	6.8	5.0
Unknown & Ill-Defined Sites	0.1	0.1	3.7	2.4	10.0	8.4	25.2	23.3	53.3	50.8	138.3	63.0	105.3	152.7	12.6	12.3
TOTAL	36.8	40.8	166.7	251.1	481.4	579.2	1321.5	1071.4	2865.8	1713.2	4360.5	2341.6	5200.0	3147.8	584.9	498.4

B.C. Cancer Statistics 1986

Age Standardized Incidence (per 100,000) by Sex

	Male					Female				
	1982	1983	1984	1985	1986	1982	1983	1984	1985	1986
Lip	2.8	2.9	3.0	2.8	2.5	0.2	0.6	0.4	0.7	0.4
Tongue	2.0	2.0	2.3	1.7	1.8	1.2	1.3	1.4	1.3	1.0
Mouth	3.4	3.2	3.7	3.5	2.9	2.0	2.1	2.0	2.7	1.5
Pharynx	3.6	4.1	4.1	4.3	4.2	1.9	1.3	1.7	1.7	1.5
Esophagus	4.1	4.3	4.2	4.5	4.6	2.1	1.8	1.7	2.1	1.5
Stomach	12.1	11.9	10.7	11.7	10.5	6.7	5.7	5.0	6.5	5.7
Small Intestine	0.6	0.6	1.1	0.8	1.1	0.6	0.5	0.6	0.8	0.6
Colon	24.2	24.0	23.9	25.6	24.3	24.0	23.9	25.8	25.2	24.2
Rectum	18.0	14.6	17.3	17.7	17.8	11.8	12.7	13.1	14.8	13.0
Liver	2.9	3.0	2.6	2.9	4.1	1.7	1.6	1.5	1.6	1.8
Gallbladder	2.2	1.9	1.6	1.3	1.9	2.5	2.8	2.2	2.0	2.6
Pancreas	10.1	9.4	7.8	8.3	8.3	6.9	7.6	5.9	6.1	6.0
Larynx	5.2	5.9	5.1	4.3	5.0	0.4	1.1	1.2	0.5	0.4
Trachea, Bronchus, Lung	61.4	59.5	60.1	60.5	58.7	26.0	28.6	30.1	27.8	30.9
Bone, Connective Tissue	2.9	2.9	2.5	3.5	3.0	2.0	2.0	2.5	1.3	2.4
Melanoma-Skin	7.9	9.3	8.1	10.6	9.4	8.7	10.5	9.4	12.8	10.3
Other Skin	114.2	118.8	126.3	138.5	139.4	87.8	98.8	95.2	103.7	104.8
Breast	0.9	0.5	0.5	0.5	0.3	76.3	81.2	76.3	84.6	82.4
Cervix	0.0	0.0	0.0	0.0	0.0	7.6	9.0	6.6	8.2	7.1
Uterus	0.0	0.0	0.0	0.0	0.0	17.1	16.1	17.3	17.3	16.1
Ovary	0.0	0.0	0.0	0.0	0.0	13.4	12.7	16.6	12.9	12.0
Other Female Genital Organs	0.0	0.0	0.0	0.0	0.0	1.0	1.8	2.0	1.8	2.2
Prostate	58.8	56.2	57.5	63.7	65.7	0.0	0.0	0.0	0.0	0.0
Testis	3.2	4.2	4.3	3.9	4.3	0.0	0.0	0.0	0.0	0.0
Bladder	17.1	16.1	14.6	13.2	13.3	5.5	5.5	4.9	4.5	4.4
Kidney	7.7	8.0	9.5	7.8	7.8	3.4	4.0	4.0	5.1	5.0
Brain	6.5	6.2	8.9	6.1	5.6	3.7	3.9	4.0	4.9	4.0
Thyroid	1.7	1.8	1.6	1.1	1.7	2.9	3.5	3.6	3.5	4.2
Non-Hodgkin's Lymphoma	11.0	11.0	11.7	11.8	12.6	10.5	10.0	7.6	8.5	8.1
Hodgkin's Disease	3.1	2.6	3.2	3.4	2.3	1.7	2.0	2.9	1.5	2.3
Multiple Myeloma	3.7	3.4	4.0	3.3	3.5	3.1	3.2	3.1	2.8	2.4
Leukemia: Acute Lymphatic	1.4	2.0	1.8	2.3	1.9	0.7	1.4	1.3	1.0	1.2
Chronic Lymphatic	2.0	2.9	3.2	2.9	3.7	1.7	1.4	2.4	0.9	2.2
Acute Granulocytic	1.2	1.1	2.2	1.1	1.2	1.9	1.3	1.6	1.3	0.9
Chronic Granulocytic	1.5	0.9	1.5	0.8	1.5	1.0	1.2	0.8	0.9	0.8
Other & Unspecified	3.2	2.3	2.4	1.7	1.9	1.7	1.5	1.4	1.2	1.8
Other Primary Sites	3.9	4.8	4.6	4.6	3.9	2.5	3.7	3.2	2.5	3.7
Unknown & Ill-Defined Sites	11.6	11.6	10.8	8.7	9.4	12.1	10.0	9.9	9.3	8.3
TOTAL	415.9	413.9	426.6	439.2	440.0	354.6	376.2	369.4	384.3	378.2

Cancer Deaths by Sex and Age-Group

	0 - 34		35 - 44		45 - 54		55 - 64		65 - 74		75 - 84		85 - UP		TOTAL	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Lip	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Tongue	0	0	1	0	2	0	9	3	7	3	6	3	1	2	26	11
Mouth	0	0	1	0	1	0	5	6	7	3	2	3	0	3	16	15
Pharynx	1	0	4	0	4	2	8	4	4	7	4	2	0	0	25	15
Esophagus	0	0	1	0	3	2	20	3	32	13	17	15	7	7	80	40
Stomach	1	1	4	3	8	3	36	7	47	26	49	33	16	13	161	86
Small Intestine	0	0	0	0	0	0	0	1	3	0	1	4	1	1	5	6
Colon	2	1	3	7	29	12	53	29	85	70	38	75	0	33	210	227
Rectum	0	0	2	0	5	2	19	12	31	14	16	13	7	15	80	56
Liver	2	4	3	2	3	1	16	8	17	9	17	13	4	6	62	43
Gallbladder	0	0	0	0	0	1	7	4	13	7	9	15	1	7	30	34
Pancreas	0	1	4	4	8	10	52	19	56	44	41	39	11	14	172	131
Larynx	0	0	0	0	4	1	15	0	10	5	8	1	0	0	37	7
Trachea, Bronchus, Lung	3	2	12	14	65	52	190	124	345	170	269	92	34	36	918	490
Bone, Connective Tissue	4	4	1	5	2	0	6	3	3	3	2	3	3	0	21	18
Melanoma-Skin	2	3	9	3	3	3	12	1	5	3	5	7	0	0	36	20
Other Skin	0	0	0	0	0	0	0	0	1	0	5	0	1	1	7	1
Breast	0	7	0	27	0	64	0	108	0	143	2	94	0	50	2	493
Cervix	0	3	0	5	0	3	0	8	0	12	0	7	0	1	0	39
Uterus	0	0	0	0	0	1	0	10	0	25	0	14	0	6	0	56
Ovary	0	2	0	10	0	15	0	35	0	49	0	32	0	11	0	154
Other Female Genital Organs	0	0	0	0	0	1	0	1	0	5	0	3	0	2	0	12
Prostate	0	0	0	0	3	0	35	0	122	0	169	0	57	0	386	0
Testis	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Bladder	0	0	0	1	3	0	12	6	32	7	24	7	15	13	86	34
Kidney	1	0	2	0	2	3	21	5	26	18	14	11	4	5	70	42
Brain	3	6	9	2	9	5	29	10	21	16	9	7	1	1	81	47
Thyroid	0	0	0	0	1	0	0	0	0	1	1	1	2	1	4	3
Non-Hodgkin's Lymphoma	5	1	6	4	6	7	20	8	25	19	22	28	5	8	89	75
Hodgkin's Disease	0	4	2	1	3	0	3	0	1	0	3	1	0	0	12	6
Multiple Myeloma	0	0	0	0	3	2	8	8	18	16	16	12	6	6	51	44
Leukemia: Acute Lymphatic	5	1	1	0	0	1	0	1	1	1	2	0	0	2	9	6
Chronic Lymphatic	0	0	1	0	0	0	8	0	3	1	6	6	3	5	21	12
Acute Granulocytic	0	4	0	1	0	3	4	7	8	2	3	0	2	3	17	20
Chronic Granulocytic	1	2	2	2	0	0	3	0	3	2	3	2	1	2	13	10
Other & Unspecified	2	1	3	2	2	1	9	4	11	7	5	10	0	6	32	31
Other Primary Sites	5	3	1	5	9	8	13	15	29	26	22	19	6	20	85	96
Unknown & Ill-Defined Sites	2	2	3	2	9	5	38	22	55	46	46	40	14	26	167	143
TOTAL	39	52	75	100	187	208	651	472	1022	773	837	612	202	306	3013	2523

Mortality Rates (per 100,000) by Sex and Age-Group

	0 - 34		35 - 44		45 - 54		55 - 64		65 - 74		75 - 84		85 - UP		TOTAL	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Lip	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.3	0.0	0.0	0.0	0.1	0.0
Tongue	0.0	0.0	0.5	0.0	1.3	0.0	6.7	2.1	7.2	2.5	13.6	5.0	10.5	9.9	1.8	0.8
Mouth	0.0	0.0	0.5	0.0	0.7	0.0	3.7	4.2	7.2	2.5	4.5	5.0	0.0	14.8	1.1	1.0
Pharynx	0.1	0.0	1.8	0.0	2.7	1.4	5.9	2.8	4.1	5.9	9.1	3.3	0.0	0.0	1.7	1.0
Esophagus	0.0	0.0	0.5	0.0	2.0	1.4	14.8	2.1	32.8	11.0	38.5	24.9	73.7	34.5	5.6	2.7
Stomach	0.1	0.1	1.8	1.4	5.3	2.1	26.7	5.0	48.2	22.0	111.1	54.7	168.4	64.0	11.3	5.9
Small Intestine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	3.1	0.0	2.3	6.6	10.5	4.9	0.3	0.4
Colon	0.3	0.1	1.4	3.3	19.3	8.4	39.3	20.5	87.1	59.2	86.2	124.4	0.0	162.6	14.7	15.6
Rectum	0.0	0.0	0.9	0.0	3.3	1.4	14.1	8.5	31.8	11.8	36.3	21.6	73.7	73.9	5.6	3.8
Liver	0.3	0.5	1.4	0.9	2.0	0.7	11.9	5.7	17.4	7.6	38.5	21.6	42.1	29.6	4.3	2.9
Gallbladder	0.0	0.0	0.0	0.0	0.0	0.7	5.2	2.8	13.3	5.9	20.4	24.9	10.5	34.5	2.1	2.3
Pancreas	0.0	0.1	1.8	1.9	5.3	7.0	38.5	13.4	57.4	37.2	93.0	64.7	115.8	69.0	12.0	9.0
Larynx	0.0	0.0	0.0	0.0	2.7	0.7	11.1	0.0	10.2	4.2	18.1	1.7	0.0	0.0	2.6	0.5
Trachea, Bronchus, Lung	0.4	0.3	5.5	6.6	43.2	36.3	140.7	87.7	353.5	143.8	610.0	152.6	357.9	177.3	64.1	33.6
Bone, Connective Tissue	0.5	0.5	0.5	2.4	1.3	0.0	4.4	2.1	3.1	2.5	4.5	5.0	31.6	0.0	1.5	1.2
Melanoma-Skin	0.3	0.4	4.1	1.4	2.0	2.1	8.9	0.7	5.1	2.5	11.3	11.6	0.0	0.0	2.5	1.4
Other Skin	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	11.3	0.0	10.5	4.9	0.5	0.1
Breast	0.0	0.9	0.0	12.7	0.0	44.7	0.0	76.4	0.0	121.0	4.5	155.9	0.0	246.3	0.1	33.8
Cervix	0.0	0.4	0.0	2.4	0.0	2.1	0.0	5.7	0.0	10.2	0.0	11.6	0.0	4.9	0.0	2.7
Uterus	0.0	0.0	0.0	0.0	0.0	0.7	0.0	7.1	0.0	21.2	0.0	23.2	0.0	29.6	0.0	3.8
Ovary	0.0	0.3	0.0	4.7	0.0	10.5	0.0	24.8	0.0	41.5	0.0	53.1	0.0	54.2	0.0	10.6
Other Female Genital Organs	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.7	0.0	4.2	0.0	5.0	0.0	9.9	0.0	0.8
Prostate	0.0	0.0	0.0	0.0	2.0	0.0	25.9	0.0	125.0	0.0	383.2	0.0	600.0	0.0	27.0	0.0
Testis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
Bladder	0.0	0.0	0.0	0.5	2.0	0.0	8.9	4.2	32.8	5.9	54.4	11.6	157.9	64.0	6.0	2.3
Kidney	0.1	0.0	0.9	0.0	1.3	2.1	15.6	3.5	26.6	15.2	31.7	18.2	42.1	24.6	4.9	2.9
Brain	0.4	0.8	4.1	0.9	6.0	3.5	21.5	7.1	21.5	13.5	20.4	11.6	10.5	4.9	5.7	3.2
Thyroid	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.8	2.3	1.7	21.1	4.9	0.3	0.2
Non-Hodgkin's Lymphoma	0.6	0.1	2.8	1.9	4.0	4.9	14.8	5.7	25.6	16.1	49.9	46.4	52.6	39.4	6.2	5.1
Hodgkin's Disease	0.0	0.5	0.9	0.5	2.0	0.0	2.2	0.0	1.0	0.0	6.8	1.7	0.0	0.0	0.8	0.4
Multiple Myeloma	0.0	0.0	0.0	0.0	2.0	1.4	5.9	5.7	18.4	13.5	36.3	19.9	63.2	29.6	3.6	3.0
Leukemia: Acute Lymphatic	0.6	0.1	0.5	0.0	0.0	0.7	0.0	0.7	1.0	0.8	4.5	0.0	0.0	9.9	0.6	0.4
Chronic Lymphatic	0.0	0.0	0.5	0.0	0.0	0.0	5.9	0.0	3.1	0.8	13.6	10.0	31.6	24.6	1.5	0.8
Acute Granulocytic	0.0	0.5	0.0	0.5	0.0	2.1	3.0	5.0	8.2	1.7	6.8	0.0	21.1	14.8	1.2	1.4
Chronic Granulocytic	0.1	0.3	0.9	0.9	0.0	0.0	2.2	0.0	3.1	1.7	6.8	3.3	10.5	9.9	0.9	0.7
Other & Unspecified	0.3	0.1	1.4	0.9	1.3	0.7	6.7	2.8	11.3	5.9	11.3	16.6	0.0	29.6	2.2	2.1
Other Primary Sites	0.6	0.4	0.5	2.4	6.0	5.6	9.6	10.6	29.7	22.0	49.9	31.5	63.2	98.5	5.9	6.6
Unknown & Ill-Defined Sites	0.3	0.3	1.4	0.9	6.0	3.5	28.1	15.6	56.4	38.9	104.3	66.3	147.4	128.1	11.7	9.8
TOTAL	5.0	6.8	34.5	47.0	124.3	145.2	482.2	333.8	1047.1	654.0	1898.0	1014.9	2126.3	1507.4	210.5	173.0

B.C. Cancer Statistics 1986

Age Standardized Mortality (per 100,000) by Sex

	Male					Female				
	1982	**1983**	**1984**	**1985**	**1986**	**1982**	**1983**	**1984**	**1985**	**1986**
Lip	0.1	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
Tongue	1.1	1.0	1.2	0.6	1.4	0.6	0.4	0.5	0.4	0.5
Mouth	1.2	1.3	0.8	0.9	0.8	0.5	0.6	0.4	0.3	0.7
Pharynx	1.3	1.8	2.1	1.8	1.4	0.7	0.5	0.7	0.4	0.8
Esophagus	3.8	4.2	4.7	4.6	4.1	1.9	2.0	2.0	1.4	1.9
Stomach	8.3	8.6	7.7	7.1	8.3	4.4	4.5	3.7	4.8	4.0
Small Intestine	0.8	0.1	0.4	0.2	0.2	0.3	0.4	0.2	0.4	0.3
Colon	11.6	11.4	13.6	11.2	11.2	10.9	11.4	11.2	11.2	10.8
Rectum	5.1	5.7	4.3	4.3	4.1	1.9	2.9	3.5	2.9	2.6
Liver	2.8	2.8	2.5	3.1	3.2	1.6	1.7	1.1	1.2	2.2
Gallbladder	1.5	1.2	1.4	1.3	1.5	1.9	1.5	2.2	2.0	1.6
Pancreas	9.5	9.2	7.7	8.2	9.0	6.1	6.9	7.6	6.1	6.4
Larynx	2.0	1.8	1.9	1.5	2.0	0.2	0.5	0.1	0.3	0.3
Trachea, Bronchus, Lung	49.1	45.7	51.6	48.6	47.1	18.8	21.2	20.6	21.9	25.0
Bone, Connective Tissue	1.3	1.2	1.5	1.3	1.3	1.3	0.9	1.2	1.0	1.1
Melanoma-Skin	2.2	1.8	1.5	2.2	2.0	1.8	1.3	1.9	1.3	1.1
Other Skin	0.8	0.7	0.8	0.2	0.3	0.7	0.5	0.2	0.3	0.0
Breast	0.2	0.0	0.1	0.2	0.1	25.5	24.2	23.4	24.8	25.4
Cervix	0.0	0.0	0.0	0.0	0.0	3.6	2.2	2.2	2.5	2.0
Uterus	0.0	0.0	0.0	0.0	0.0	3.1	2.8	2.9	2.2	2.6
Ovary	0.0	0.0	0.0	0.0	0.0	8.9	7.2	8.7	7.3	7.9
Other Female Genital Organs	0.0	0.0	0.0	0.0	0.0	0.6	0.2	0.6	0.4	0.6
Prostate	16.5	14.9	16.7	16.3	19.0	0.0	0.0	0.0	0.0	0.0
Testis	0.2	0.2	0.3	0.4	0.1	0.0	0.0	0.0	0.0	0.0
Bladder	5.1	4.7	4.3	5.0	4.3	1.4	0.9	1.6	1.7	1.5
Kidney	3.5	3.5	4.3	3.8	3.7	1.8	1.8	2.1	1.6	2.0
Brain	5.3	4.1	5.6	5.7	4.6	3.3	3.1	2.9	3.5	2.6
Thyroid	0.5	0.3	0.5	0.1	0.2	0.7	0.8	0.6	0.4	0.1
Non-Hodgkin's Lymunoma	4.5	5.7	4.7	5.9	4.7	3.5	4.6	4.0	4.4	3.7
Hodgkin's Disease	0.8	0.4	0.4	0.2	0.7	0.5	0.3	0.2	0.6	0.4
Multiple Myeloma	2.8	1.9	2.4	2.5	2.6	1.6	2.1	2.4	2.3	2.1
Leukemia: Acute Lymphatic	0.8	0.7	0.7	0.5	0.6	0.6	0.1	0.8	0.7	0.3
Chronic Lymphatic	1.4	1.3	1.5	1.3	1.1	0.7	0.8	0.9	0.9	0.5
Acute Granulocytic	1.1	0.9	1.3	1.3	0.8	1.7	1.0	1.5	0.9	1.1
Chronic Granulocytic	0.6	0.5	1.1	0.8	0.6	0.5	1.0	0.7	0.5	0.6
Other & Unspecified	2.6	2.7	3.3	2.1	1.7	1.3	1.2	1.6	1.6	1.5
Other Primary Sites	2.8	3.9	4.1	4.4	4.0	3.4	3.3	5.0	5.0	4.6
Unknown & Ill-Defined Sites	5.6	5.0	5.9	5.9	6.6	4.6	5.6	6.9	6.3	6.8
TOTAL	156.5	149.1	160.5	153.5	155.5	120.7	120.3	126.4	123.7	125.7

British Columbia Cancer Research Centre

The British Columbia Cancer Research Centre

The British Columbia Cancer Research Centre was established in 1974 by the British Columbia Cancer Foundation, with the support and cooperation of the University of British Columbia; the National Cancer Institute, which is the research arm of the Canadian Cancer Society; and the Cancer Control Agency of British Columbia.

Cancer research is playing an increasingly important role in diagnosis and treatment of the disease and the Research Centre today works in close collaboration with the Cancer Control Agency of B.C. which is responsible for all diagnosis and treatment in the Province.

Research at the Centre is conducted by some forty scientists and 130 support staff, including Ph.D's, graduate students, technologists and secretaries. Many of the research findings of our scientists and treatment protocols developed from their work are winning international recognition.

This has placed the B.C. Cancer Research Centre in the forefront of cancer research and treatment in the world. It has been said by cancer specialists elsewhere that if a particular cancer treatment is not available in Vancouver, it is simply not available anywhere.

There are seven Divisions/Units in the Research Centre, either focusing on specific sites or types of cancer; analyzing the origins and development of the disease; or concentrating on new methods of treatment.

Medical Biophysics Unit
Biological effects of ionizing radiation; improvements in radiotherapy; studies in the combining of chemotherapy and radiation.

Epidemiology, Biometry, Occupational Oncology
Three main subject areas are: geographic mapping of cancer in B.C., the epidemiology of breast disease in B.C., risk factors for melanoma.

Advanced Therapeutics
Seeks new methods of diagnosis and advances in the administration of chemotherapy.

Cancer Endocrinology
The application of hormonal therapy to various cancer sites.

Cancer Imaging
Study of computerized screening of cancer cells. The application of computer technology to microscopy to develop new equipment that will make possible mass screening of population segments at affordable costs.

Terry Fox Laboratory for Hematology/Oncology
Studies of cancer of the blood/diagnosis and treatment.

Environmental Carcinogenesis
The role of environment, lifestyle and genetics in the development of cancer.

Photograph: (previous page) Denise McDougal, the research technologist who operates the FACS in the Medical Biophysics Unit, checking the sample stream of the instrument. A schematic flow diagram is shown on the outside cover of the Annual Reports.

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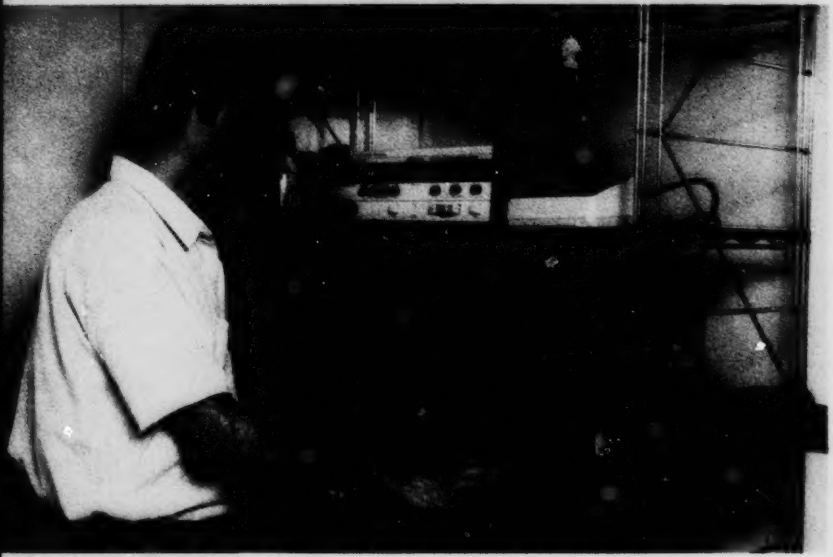
Introduction

The research programs of the Medical Biophysics Unit continue to encompass a range of subjects from basic studies of the mechanisms of action of radiation and of chemical agents potentially useful for cancer treatment, to the application of new treatment modalities or strategies in the clinic. The excellent spirit of cooperation and the mutual interest that exists between our unit and the Divisions of Radiation Oncology and Medical Oncology (CCABC) have been extremely positive factors that have allowed the results of our research to be rapidly tested in the clinic. Clinical studies of pion therapy, of tumour blood flow manipulation and of chemotherapy treatments optimized in our tumour model system, are three examples of new treatment approaches which have been suggested by our research, and which are now being applied clinically, all with very interesting results.

We shall miss our interaction with Dr. Charles Ludgate of the Division of Radiation Oncology, who will move to the Victoria Cancer Clinic this fall. Dr. Ludgate has for several years organized the monthly "Rads and Rats" meetings between the clinical staff (particularly Radiation Oncology and Medical Oncology) and Medical Biophysics staff. These meetings have been very successful and well attended and have done much to stimulate the interaction between the clinical and research groups. Fortunately, Dr. Brian Acker will assume the responsibility for organizing the "Rads & Rats" meetings in the future. During the past year, Dr. Acker has spent half of his time on research, in collaboration with Dr. David Chaplin (their work on blood flow studies is described below). This arrangement, initiated in 1987, will allow interested Radiation Oncology staff to devote a portion of their time to research. We are delighted with this arrangement and wish to acknowledge the efforts of Dr. Stuart Jackson, Head of the Division of Radiation Oncology, Dr. George Goodman, Head of Developmental Radiotherapy and Dr. David Klaassen, the Director of the Cancer Control Agency, all of whom supported this initiative.

Our professional staff continues to be involved in teaching and supervision of graduate students at UBC, where all have academic appointments. They also serve on a variety of national and international professional organizations including editorial boards, councils of scientific societies, grant review panels and a number of



Mark Skwarchuk, a graduate student in Medical Biophysics is shown with the apparatus which provides synchronously dividing cells used in the low radiation dose studies.

committees, advisory groups, etc. Dr. Ralph Durand is Associate Editor of both *Cancer Research* and *Radiation Research* and has just assumed the chairmanship of NCIC Grant Panel E. Dr. Peggy Olive, having just completed a term as a member of the Clinical Sciences Study Section at NIH (U.S.) is now a member of their Radiation Study Section (grant review panel). This year Dr. Chaplin completes his term as member of the MRC cancer panel. Members of staff also frequently serve on site review teams to evaluate programs at other Canadian and U.S. institutions.

The staff, including post-doctoral fellows and graduate students, have all presented papers at a number of national and intertional scientific meetings and symposia during the past year, often as invited speakers. They have also benefitted from the visits to our laboratories by many distinguished scientists and oncologists from other institutions around the world.

Each week, the professional staff, technical staff and students in Medical Biophysics meet to discuss research in progress, with one or two individuals presenting recent results of interest. During the past year, these meetings have been coordinated by Dr. Andrew Minchinton and Dr. Martin Trotter, both of whom have done an excellent job of organizing these extremely valuable sessions.

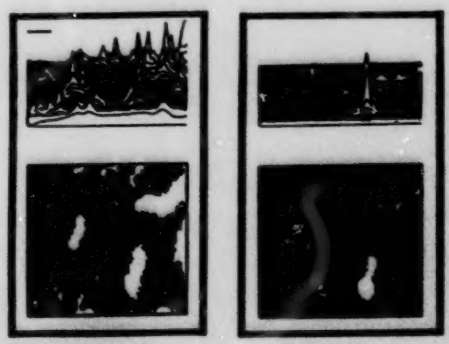
The following report gives a brief overview of several projects which are in progress at the present time. Further detail can be found in the Unit's published papers which are listed under Medical Biophysics.

Developing New Fluorescent Probes for Locating Hypoxic Tumour Cells

P. Olive and M. Trotter

Rapidly growing tumour cells often outgrow their blood supply. The resulting poorly oxygenated (hypoxic) tumour cells are generally resistant to treatment with conventional cancer therapies. Our goal is to develop new fluorescent probes for identifying hypoxic cells and then use flow cytometry and fluorescence imaging methods to locate and quantify hypoxic cells in tumours. Results from these studies are improving our basic understanding of tumour biology, and may ultimately help us determine which human tumours are likely to contain hypoxic cells.

This year, two new fluorescent probes have been identified and characterized in multicell spheroids and in mouse tumour models. A carbocyanine drug, DiOC$_7$(3) rapidly binds to cells close to blood vessels, producing a gradient of green fluorescence. Tumour cells close to blood supply are about 100 times more fluorescent than cells distant from the vessels. Dr. Martin Trotter has been using this stain, together with the blue-fluorescent stain Hoechst 33342 to identify regions of tumours which undergo fluctuations in tumour blood flow. Using a new fluorescence image processing system (FIPS), he was able to chart the position of blood vessels in frozen sections of tumour cells. If these two dyes are injected 20 minutes apart, most of the cells next to blood vessels are stained both blue and green. However, about 8% of the vessels contain only one of the dyes because these blood vessels have closed during the 20 minute interval between injection of the two dyes. These areas of "acute" hypoxia are of



Closure of blood vessels in a mouse tumour. Open blood vessels stained with Hoechst 33342 are seen as white areas (left panel). 20 minutes later, when DiOC$_7$(3) stain is used several vessels have closed (right panel).

particular interest in targeting new antitumour treatments.

A second stain with an entirely different mechanism of action is being evaluated as a fluorescent "redox" probe. Hydroethidine is a non-fluorescent molecule which is metabolized in well-oxygenated cells to a red fluorescent drug which binds to DNA. We have found that hypoxic cells are less able to metabolize this compound, so these cells remain only dimly fluorescent. This stain is now being evaluated as an hypoxia probe in mouse tumours.

Relation Between DNA Repair Capacity and the Extracellular Environment

P. Olive

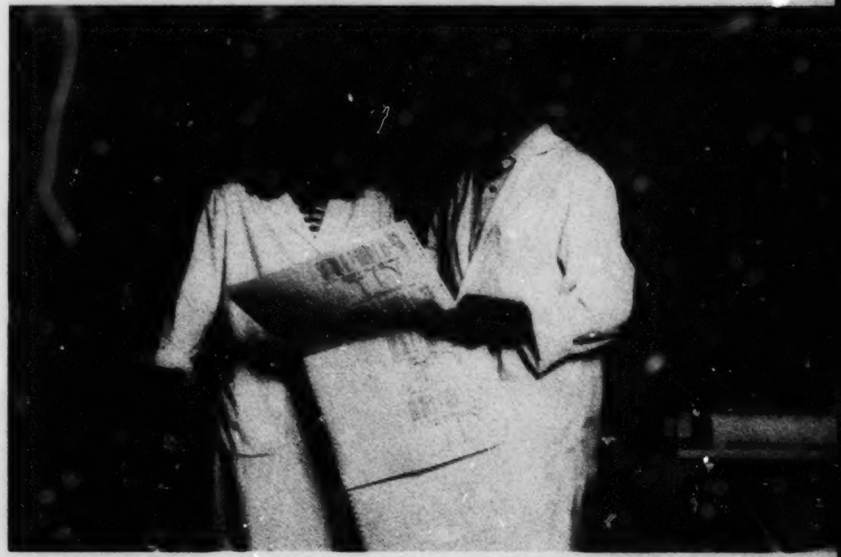
The environment of a tumour cell can change dramatically through its life history. The cell environment is known to influence important processes in the nucleus such as DNA replication and gene transcription. It is thought that signals originate in the cell membrane when membrane receptors recognize special "extracellular matrix" molecules. These signals pass through fibres in the cell to the nucleus, but how they ultimately influence processes within the cell nucleus is not known. Susan MacPhail has found that the organization of DNA in the nucleus often changes when the environment of a cell changes. Using the new method of microelectrophoresis, Angela Chan has observed differences in the radiation sensitivity of individual cells grown in different environments. These changes in DNA "packaging" appear to influence the ability of cells to recover from damage by ionizing radiation and some drugs. Preliminary results obtained by Carissa Cu point to the involvement of an enzyme called Topoisomerase II, which is required for DNA replication and possibly DNA repair.

Hypoxia-Targetted Chemotherapy

D. Chaplin and B. Acker

The usual goal of chemotherapy is to find and exploit some unique metabolic difference between the "invading" and normal cell populations. The classic example is the action of penicillin on cell wall synthesis, a process specific for bacteria. However, the distinction between normal and malignant cells is more elusive. To date, most cancer chemotherapeutic agents have been designed to exploit subtle differences in cell proliferation rate and biochemistry that exist between normal and neoplastic cells. However, since such differences are not absolute, damage to normal tissues limits drug utility. Before new directions in chemotherapy can be established, there is a need to identify or generate exploitable differences between malignant and normal tissue.

In the last few years, we have attempted to exploit physiological differences between cancer and normal tissue. Results obtained have clearly shown that concurrent administration of chemotherapeutic drugs which are known to be toxic to hypoxic cells, and vasodilating drugs which are known to reduce tumour blood flow is therapeutically advantageous. Further studies completed this year have confirmed our initial findings and indicate a potential new strategy for increasing the efficiency of certain cancer chemotherapeutic agents in solid tumours. This work has stimulated major research programs in both the U.S. and Europe. Initial clinical studies evaluating this approach are now underway at the CCABC and in the U.K. This work has been carried out with the skilled assistance of Mr. Douglas Aoki and Ms. Sandy Mills.



Nancy LePard and Ralph Durand reviewing data from the FACS facility.

The Nature of Tumour Hypoxia

D. Chaplin, A. Minchinton, P. Olive, M. Trotter and R. Durand

Over the past 3 years, we have used novel cell sorting and histological techniques to study the cause of tumour hypoxia. Our studies have provided direct evidence that tumour hypoxia can result from transient fluctuations in blood flow. Most therapies used to overcome tumour hypoxia in clinical radiation therapy are based on the idea that hypoxia arises distant from blood vessels as a result of oxygen utilization by the cells closest to the vessel itself. The fact that hypoxia can also result because of a temporary shutdown or occlusion of a tumour blood vessel could have important implications to the methods used to improve current radiation therapy treatment. More recently, we have been evaluating novel therapeutic interventions designed to reduce or eliminate such hypoxia. Preliminary results with drugs such as angiotensin II and nicotinamide indicate that these agents may have a role in radiation therapy. This work has been carried out with the skilled assistance of Mr. Douglas Aoki, Ms. Sandy Mills and Mr. William Grulkey.

Selection of Chemotherapy Combinations to Overcome Drug Resistance

R. Durand

Dr. Durand's research program continues to exploit cell sorting capabilities developed in the Research Centre. Two quite different research directions are currently under pursuit: more effective utilization of available chemotherapeutic agents, and development of predictive assays for clinical response to treatment.

The rationale for this work follows from the clinical observation that most human tumours will initially respond to drug treatment, yet few tumours can be cured by drugs alone. Resistance to the drug is generally implicated as the cause of treatment failure, but it is seldom possible to know when, where, or why resistant cells appear within the tumour. This information can be determined in laboratory models, including the spheroid system with which Dr. Durand and his colleagues primarily work, and additionally, in murine tumour systems used by other investigators in the Research Centre.

Postdoctoral fellows Dr. Andrew Minchinton (left) and Dr. Martin Trotter are pictured together at the laser doppler flowmetry workstation. Both scientists are using this equipment to measure tumour and normal tissue blood flow in experimental systems.

Using these cell sorting techniques, our FACS operator, Denise McDougal, can process spheroid or tumour specimens to determine which cell subpopulations are effectively killed by each drug, and which are resistant. In collaboration with Sandra Vanderbyl and Charlene McCann, time dependent changes in responsiveness of the tumour model system to continuing drug treatments is under study. Concurrent experiments, primarily conducted by Nancy LePard, are addressed at understanding the mechanisms of action and interaction of chemotherapeutic agents. During all these studies, Dr. Durand's group continues to develop methods to more rapidly predict whether treatment is effective.

Results from Dr. Durand's laboratory-based studies are already being translated to the clinic, where Dr. James Goldie, Director, Medical Oncology, CCABC and his colleagues have begun to investigate drug combinations suggested by the laboratory work. We are highly optimistic that the unique environment of the B.C. Cancer Research Centre, in which laboratory and clinical programs (at the CCABC) run simultaneously and pose questions and answers for each other, will lead to significantly improved cancer treatment.

Metal Complexes: Potential Radiosensitizing and Chemotherapy Compounds

K. Skov

In order to eliminate those cells in tumours which are resistant to radiotherapy due to lack of oxygen, several approaches have been taken by radiobiologists, including development of drugs.

Dr. Skov and her group have been exploring the use of metal-containing compounds to attack the hypoxic problem in several ways:

1. Some metal complexes can mimic oxygen as sensitizers. A hydroxynaphthoquinone complex of nickel shows many properties similar to known radiosensitizers and its analogues will be further assessed *in vivo* and for mechanisms. Donna Ruta has been screening other complexes in tumours in collaboration with Roberts Pharmaceuticals Inc. In addition, work is proceeding using metal to bind known radiosensitizers to DNA. These projects are showing promise. Graduate student Peter Chan has completed his thesis work on the use of Ruthenium for this purpose, and his project led to a patent application as well as to several publications. Some of the platinum complexes synthesized in collaboration with Dr. N. Farrell, University of Vermont, have also resulted in

a patent application. The interaction of platinum compounds already in clinical use, with low radiation doses is being explored by Dr. Mladen Korbelik (Cancer Imaging) and Susan MacPhail.

2. The latter metal complexes are of interest also because they are more toxic to hypoxic than oxic cells even without radiation. Furthermore, it is possible to use other non-metal targetting agents, and Hans Adomat is synthesizing and testing such compounds. Don Yapp, a new graduate student in Chemistry, will explore the toxicity of Iridium-nitroimidazoles.

3. Finally, we are pursuing the possibility that some of our compounds enhance the hypoxic toxicity of otherwise non-selective agents, and that some of the new agents we are developing could be useful in detection of those tumours with radioresistance.

Dr. Kirsten Skov (Medical Biophysics Unit) and Dr. Brian James (Department of Chemistry, UBC) discussing with Peter Chan, PhD candidate, a new metal complex with radiosensitizing properties, which he synthesized. (Courtesy of UBC Community Relations)

Cell Inactivation at Low Radiation Doses

L. Skarsgard

Measurement of the effects of radiation on cultured cells has long been one of the standard laboratory procedures for evaluating the effectiveness of new anti-tumour strategies in radiation therapy. One of the shortcomings of this system, however, has been the difficulty of making accurate measurements of cell killing at low doses, 2-3 Gy, comparable to the doses used in daily radiotherapy treatments. We have used the cell sorter (FACS) to improve the accuracy of measurement in this dose range. The resultant precision has led to the discovery of "fine structure" in the radiation response at low dose, structure which has not previously been discernable. We are still investigating the basis of this structure, though we expect that it is due, at least in part, to cells of different sensitivity in the population. The importance of these observations to radiation therapy, stems from the fact that our measurements show quite significant differences in cell killing at these doses, in comparison to the effects one would expect from interpretations based on the earlier, higher dose measurements. Since cultured cell data provide a guide often used by radiotherapists in situations where a new radiotherapy treatment schedule is to be explored, it is important to obtain the most accurate possible measurement of the cell killing effect in the dose range of 2-3 Gy, commonly used in radiotherapy.

This position was recently reinforced after presentation of our results at a meeting of European and North American radiobiologists involved in the development and testing of mathematical models of the effects of radiation, relevant to human exposure. This group had been asked to provide guidance to the U.S. Dept. of Energy (DOE) and the Commission of European Communities (CEC) regarding new research initiatives which DOE and CEC should be fostering. A high priority was given, at this meeting, to expanding low dose studies using the methods we described. This research is also contributing to a better fundamental understanding of the effects of radiation on cell populations. The present focus of our effort is on the low dose response of cells at different stages of the cell division cycle.

The staff involved in this program includes Drs. Skarsgard and Durand, technicians Doug Wilson and Denise McDougal, and Mark Skwarchuk, a graduate student.

Acknowledgements

The Medical Biophysics Unit receives core support from the B.C. Cancer Foundation. In addition to this, research operating grants for 1987-88 were received from a number of sources: the National Cancer Institute of Canada, the Medical Research Council, the National Institutes of Health (U.S.) and the B.C. Health Care Research Foundation. Research contracts were also negotiated with Roberts Pharmaceuticals, Warner-Lambert, and Ciba-Geigy.

Research in Radiation Physics

Progress Report: Theoretical investigation of interaction of radiations

In 1987, our theoretical investigation of the effect of mixed radiations was extended to several other areas. Although this study originates from the TRIUMF pion therapy project where the pion beam has relative biological effectiveness (RBE) that varies significantly with depth, the findings are much more general because most radiations used clinically are either contaminated or contain components of a broad energy spectrum. The theoretical development centers on an hypothesis of the existence of a common intermediate lesion produced by all radiations. Recently, *in vivo* data obtained using mouse foot skin reactions was also shown to be in good agreement with the model. This gives very strong support to the model because *in vivo* data has no explicit mathematical dose-effect relations and hence they cannot be analysed by the conventional biophysical models of radiation action. Some of the highlights of the development of the lesion additivity (LA) model during the past year are as follows.

A. Bearing of the LA concept on the general mechanism of action of radiation.

The LA concept postulates no direct interactions between the lesion produced by the radiations throughout the course of their radiation action. The initial lesions produced by two or more different radiations develop independently before arriving at the common stage. After they merge at the common stage, they will become indistinguishable as they share the same inactivation pathway leading towards the same end-point. This simple picture requires that within the usual dose range used in radiobiology, the early lesions induced by radiations are mostly isolated from one another and from those of the other radiations, so that they can develop independently. The exact nature of these early lesions is still unknown but their sizes can be estimated if the spatial interaction of these lesions is expected to affect the shape of the survival curve.

In the Theory of Dual Radiation Action using microdosimetric measurements, this interaction distance is estimated to be in the order of micrometers, which is the scale of distance required to explain the shoulder of survival curves in terms of sublethal damage occurring over a dose range of a few Gy. However, within the last decade, there are several experimental findings that are in conflict with this interpretation. These include (i) the ultra-soft X-ray experiment, and (ii) the survival curve of human fibroblast. These experiments suggest that the interaction distance between lesions is in the order of nanometers, and the shoulders of survival curves observed over a range of a few Gy are not due to interaction of lesions. A class of new models based on biological repair processes, instead of on physical interaction, have been postulated to provide good alternatives to explain these findings. The agreement of the LA model with mixed radiation results, therefore, provides strong support to these repair models by presenting strong evidence that the initial lesions induced by different radiations do not interact over distances of the order of a micrometer as postulated in the Theory of Dual Radiation Action.

B. Application of the LA concept to radiation protection.

It was shown that the current definition of dose equivalent and average quality factor used in radiation protection as defined by the International Commission of Radiation Unit and Measurement actually implies some interaction between the radiations unless the dose effect relationship for all radiations is linear. However, no interaction is specified in the reports where these definitions are stated. Furthermore, the radiation interaction required to relate the two definitions cannot be derived from published models that describe radiation interaction. It was shown that the LA concept can be used to uphold the general validity of these two basic definitions. Both the concept of dose equivalent and the linear summation of dose equivalent for a mixture can be derived logically from the LA model. Since the LA model is in good agreement with the radiobiological data, the model thus provides both theoretical and experimental support to the otherwise arbitrary definitions currently used in radiation protection.

C. Application of the LA concept to the treatment planning of high-LET radiations.

The treatment planning for conventional radiations is based on the additive dose principle when several beams are required in a plan. This implies that the effect of a combination of doses in a multi-port irradiation is equivalent to that of a single dose which is the total sum of the doses from all the beams. This is obviously valid for conventional radiation or for any radiation which has constant RBE throughout the field. However, for high-LET radiations such as pions and heavy ions, the RBE varies with the depth of penetration and so the treatment planning of these radiations cannot be based on dose. It was shown that, with the use of the LA concept, effective doses (defined as dose x RBE) are additive and hence when the physical doses are converted to effective doses, linear additivity is restored and treatment planning for high-LET radiation can proceed conveniently using the techniques that have already been developed for linear addition of physical doses for conventional radiations. Treatment plans for different types of radiations based on effective doses can also be meaningfully intercompared.

In fact, treatment plans for conventional radiations can be viewed as a particular case of effective dose plans where the RBE at all locations is unity. This helps to unify the treatment planning procedures for the new generation of particle radiation with that for conventional radiation.

Cancer Imaging

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Cancer Imaging staff assembled for a group picture. From left to right: Brian Pontifex, Mladen Korbelik, Steven Poon, Alan Harrison, Jaclyn Hung, Evan Hobenshield, Errol Samuelson, Branko Palcic, Calum MacAulay, Neal Poulin, Bruno Jaggi, Gurmail Kandola, Ingrid Spadinger, Vel Kinnie and Haluk Tezcan. Lily Haydar, Susan Grose and Gavin Thurston (who recently completed his Ph.D. studies) are not shown.

The main objective of Cancer Imaging is research and development of means to detect early cancers. This Section was instituted in Spring, 1987 as part of the Physics Division of the Cancer Control Agency of B.C. Dr. Branko Palcic, Section Head, assembled a group of young scientists, engineers and graduate students whose expertise ranges from mathematics, physics, engineering, biology to medicine. A thorough understanding of these disciplines is a necessary prerequisite for the development of sophisticated devices and procedures where computer vision and artificial intelligence is used for the detection and characterization of malignant cells.

At present, two main programs are underway. These are the analytical cytology of cervical smears and the detection of small lung cancers. Both programs are already funded by granting agencies such as the National Cancer Institute, Medical Research Council, B.C. Health Care Research Foundation, B.C. Lung Association, Vancouver Foundation, Woodward Foundation and others.

The goal of the analytical cytology of cervical smears program is to screen in a fully automated way exfoliated cervical cells for the presence of pre-malignant and malignant cells. Many studies must be carried out simultaneously before an apparatus with these capabilities can be built. These include special sample preparations and staining techniques, algorithm research, sensor and software development, research of new electronic circuits and optical designs, etc. The deposition and staining of cells must be modified so that the characteristics are matched to the properties of the best available optical sensors. Algorithms, which exploit spectral, spatial and photometric characteristics of stained cells must be found which not only recognize cells but also delineate cytoplasm and nucleus of these cells. They must also separate overlapping cells and cell clumps from single cells. Cellular features, which are extracted from recognized and delineated cells, include nuclear size and shape, amount of DNA and its distribution through the nucleus, recognition and quantification of condensed nuclear material and others.

Using a specially designed and developed apparatus, built by funds provided by the National Cancer Institute of Canada, most of the above tasks have been completed. Mr. Calum MacAulay, a Ph.D. student in Physics and Dr. Haluk Tezcan, M.D., a Ph.D. student in Pathology, have been the main force in algorithm and sample preparation development. Their work has now been tested on a large number of samples provided by Dr. George Anderson, Head of the Cytology Division, CCABC and by Dr. Nancy Kiviat, Director of Cytology, Department of Cytology, Harbourview Medical Centre in Seattle, Washington, who heads a major project in the U.S.A. designed to establish objective criteria for the classification of cervical cells.

One of the most important new projects in Cancer Imaging is the development of a new Solid State Microscope. A group of engineers, students and technicians is shown discussing the progress and future research objectives. The group is headed by Bruno Jaggi, P.Eng.

It has been recognized, however, that even the most sophisticated, present-day digital microscopes cannot provide morphometric data of cells with the precision required for routine clinical screening and classification of cells. The optical and electronic distortions produced by these devices must be reduced several fold. In addition to that, the processing speed of the images must be increased at least 100 times. For this reason, the scientists and engineers of Cancer Imaging, in collaboration with scientists from the School of Engineering Science of Simon Fraser University, have designed a new kind of quantitative microscope. This device, the Solid State Microscope, eliminates all optical elements such as lenses, prisms, mirrors and oculars. Instead, the microscope is composed of a simple lens, the objective, while

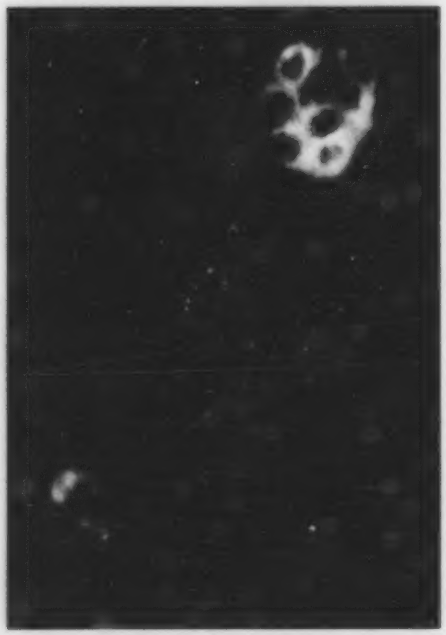
Dr. George Anderson (left), Calum MacAulay and Dr. Haluk Tezcan, discussing the latest results of the development of automated segmentation and measurements of cervical cells.

sophisticated very large scale integration (VLSI) solid state electronics constitute the remainder of the device. The advantage of the Solid State Microscope is best realized in its scanning mode, where the recognition and imaging of objects' spectral information provide means for fast, precise, and economical recognition and classification of cells. Mr. Bruno Jaggi, P.Eng. heads this project combined with a group of several young engineers and students such as Steven Poon, P.Eng., Brian Pontifex, Errol Samuelson, and others.

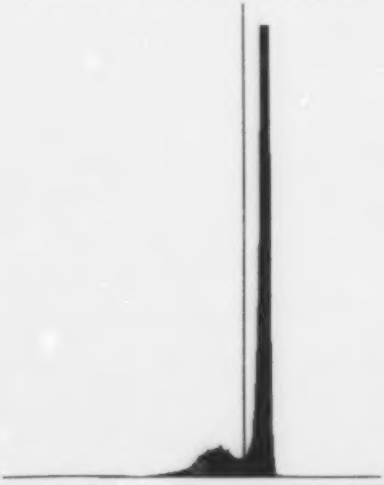
The second major program is the detection of small lung cancers. It is well-known that most lung cancers are already incurable when they are detected by conventional means such as x-rays. The overall 5-year survival of lung cancer patients is 10% or less and this figure has not changed significantly in the last twenty-five years. However, if these cancers were detected in their pre-invasive state, most of them could be completely eradicated, yielding a 5-year survival rate exceeding 90%. Thus, even a slight improvement in its early diagnosis of high risk people could make a significant impact in the management of this disease.

A group of oncologists, scientists and students in Cancer Imaging is pursuing the

Human tumor cells were exposed to a drug (Photophrin II) which preferentially accumulates in malignant cells. The drug fluoresces in bright red colour if illuminated by violet light. Malignant cells are thus clearly seen by fluorescence light. This can be used to detect small foci of malignant cells which would otherwise be occult to any other detection technique. Distribution of fluorescence is shown on the graph at the right. From such distributions the amount of the drug in each cell can be determined.



Histogram plot of 512 x 480 window at (0.0) of image



above threshold of 128: 0
# pixels at level: 296
intensity level: 34
# pixels below level: 222,197

std dev: 14,988
mean: 19
max: 123
min: 0

idea that malignant lung cancers can be detected even when they are extremely small and invisible even to a skilled endoscopist on standard white light examination. Some drugs, such as porphyrins are known to be taken up preferentially by cancerous cells. These compounds also fluoresce so that malignant foci as small as 1mm in diameter can be detected using a specially designed imaging system.

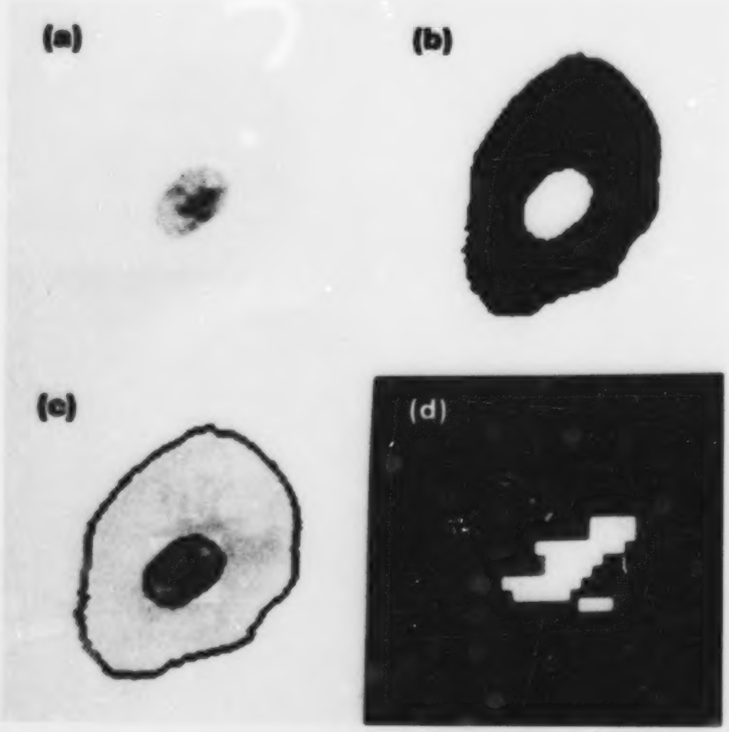
The most advanced fluorescence endoscope is being built by Professor A. Profio, Santa Barbara, University of California, which is to be delivered to the Cancer Research Centre by the Fall of 1988. Simultaneously, a special purpose video detection system is being developed by the physicists and engineers of Cancer Imaging which will be coupled to the fluorescence endoscope. The new device will be used in studies of how best to exploit the fluorescent properties of porphyrins and how to overcome the extremely high signal-to-noise ratio requirements for the detection of small tumours. This project is headed by Dr. Stephen Lam, Respiratory Division, Faculty of Medicine, U.B.C. (clinical studies) and by Dr. Mladen Korbelik, a scholar of the B.C. Health Care Research Foundation, who is responsible for *in vitro* and *in vivo* studies. Ms. Jaclyn Hung, a graduate student who has recently started her Ph.D. program in Physics, is associated with this project.

Numerous programs are pursued in Cancer Imaging in collaboration with other units in the B.C. Cancer Research Centre, various Departments of the University of British Columbia and Simon Fraser University, and Vancouver hospitals, as well as several universities and institutions throughout the world. These projects include the detection and quantitative characterization of chromosomes (a joint project with Terry Fox Laboratory); studies of perturbation of motility properties and cell division of ocular cells by chemotherapeutic drugs (Ophthalmology, Vancouver General Hospital and Keio University, School of Medicine, Tokyo, Japan); effects of low doses of ionizing radiation using different radiation modalities and sensitizers (Medical Biophysics Unit, B.C. Cancer Research Centre, Lawrence-Berkeley Laboratories, University of California, and Department of Radiation Sciences, Uppsala University, Sweden); measurements of morphometric properties of ocular melanoma cells in tissue slices (Cytology, Cancer Control Agency of B.C. and Pathology, Faculty of Medicine, McMaster University, Hamilton, Ontario); detection, characterization and classification of myeloid and lymphoid cells of child patients with acute lymphoid leukemia (Children's Hospital, Vancouver); cell perturbations induced by low frequency of magnetic fields (Ontario Hydro), and others. Sophisticated scientific equipment now available in Cancer Imaging was mostly conceived, designed, developed and built by the Section's staff. Several different apparatus have been built for other institutions in Canada, the United States and Europe. The members of Cancer Imaging have been recognized as world leaders in image cytometry of live and fluorescently stained cells.

The concept of combining the expertise of several different scientists working as a group towards a common goal appears to be effective. In the near future, new projects in the detection of early cancers by non-invasive means will be initiated. For example, a helper diagnostic tool for the breast screening program is planned. Another project under consideration is how to employ different physical principles for detection and imaging of prostate, colon and stomach cancers in their early stages.

Dr. Stephen Lam (centre right) joining Jaclyn Hung, Dr. Mladen Korbelik and Dr. Branko Palcic in experiments measuring fluorescent properties of human tumor cells.

A stained cervical cell was detected using the Cell Analyzer Imaging System. The image was captured, digitized and stored in the computer memory (a). The cell was then automatically segmented into the nucleus and cytoplasm (b), the edge around the nucleus and cytoplasm was drawn onto the original image (c) and from the original data within the nucleus, high density chromatin distribution was calculated. This is seen as white material in the expanded view of the nucleus (d). The values below the figure represent quantitative characteristics of the cell such as cell size, nuclear to cytoplasmic ratio, nuclear shape, distribution of the DNA in the nucleus and others. It is these features which discriminate between normal, pre-malignant and malignant cells.



	Feature	Values
1.	Nuclear Area	393.0
2.	Nuclear to Cytoplasmic Ratio	0.010
3.	DNA Content	320.0
4.	Mean Optical Density	0.814
5.	Normalized Variance of Mean Optical Density	0.278
6.	Circularity of the Nucleus	1.142
7.	Elongation of the Nucleus	1.439
8.	Coarseness of Nuclear Boundary	5.73
9.	Entropy of the Nucleus	3.923
10.	Energy of the Nucleus	0.001
11.	Fraction of Condensed DNA	0.181
12.	Number of Particles of Condensed DNA	2.0
13.	Condensed DNA Average Particle Size	20.0

Developmental Radiotherapy

1. PARTICLE RADIOTHERAPY

(In cooperation with Dr. E. Vogt, Director, TRIUMF - UBC; Dr. L.D. Skarsgard, Dept. of Medical Biophysics, BCCF)

01. Pion Irradiation

The preliminary studies of patients with astrocytomas grades III & IV (glioblastoma multiforme) are now complete and a prospective randomized trial comparing pions and photons is being planned. It has been determined that a dose of 36 Gy pion rads in 15 fractions represents the upper limit of normal brain tolerance for tumours of limited volume. The prospective study will use a dose of 34.5 Gy in 15 fractions to be compared with a standard photon arm of 60 Gy. It is also planned to develop a prospective randomized trial for carcinoma of the prostate. TRIUMF administration intends to upgrade the beam facilities which should increase the pion beam intensity by a factor of 6 at least. This will result in shorter patient treatment times and increase the numbers of patients treated.

02. Proton Beam Irradiation

Planning and Steering Committees are considering recommendations concerning proposals for proton therapy at TRIUMF. TRIUMF has indicated that a proton beam could be made available in late May of this year (1988) for early physics testing.

2. HYPOXIC CHEMOSENSITIZATION & TUMOUR BLOOD FLOW

(Dr. Acker, Radiation Oncology & Dr. Chaplin, Medical Biophysics, BCCRC)

Hypoxic chemosensitization includes studies (in the lab and pilot studies in humans) of the interaction of hypoxic cell cytotoxins with vasodilator drugs. The object is to enhance local radiocurability of radioresistant tumours.

In addition, studies of tumour blood flow using laser doppler flowmetry are elucidating the basic mechanisms of the effects of vasodilator agents.

3. PET SCANNING

(In cooperation with Dr. B. Pate, PET-UBC Imaging Research Centre)

In the past year Dr. H. Shirato, visiting Japanese Fellow, successfully completed a research project involving the detection of pion induced radioactivity using autoradiography and positron emission tomography. He presented a paper on the subject at the Second International Charged Particle Dosimetry Workshop at the Loma Linda University in October 1987. This new technique was shown to be capable of defining the pion stopping region with a better resolution than PET scanning. It might be useful as a complementary technique to radiographic film for pion dosimetry.

4. PREDICTIVE ASSAYS

(In cooperation with Dr. R. Durand, Dept. of Biophysics, BCCF)

Human tumour samples have been obtained and assayed for the extent of hypoxia, tumour glutathione and peroxide levels. The processing could be done satisfactorily. A prospective study for cancers of the head and neck and uterine/cervix was designed. In the study the results of the laboratory tests will be correlated with treatment outcomes and other clinically important prognostic factors. The study has received approval by the appropriate investigation and ethics committees.

5. STAFF

Dr. Dorianne Rheaume joined us in January 1988 as TRIUMF Fellow to replace Dr. C.C. Gaffney who has returned to the United Kingdom. In June 1988 the Japanese government will again sponsor another Fellow to spend a year studying pion therapy and treatment planning at TRIUMF. Dr. Yasuhiro Ogawa has his M.D. and Ph.D. degrees and is an Associate Professor in Radiology at the Kochi Medical School. Dr. B. Acker has been seconded from Radiation Oncology on a part-time basis for the year 1988.

Environmental Carcinogenesis Unit

STAFF:

H.F. Stich, Ph.D. (Wurzburg), Head, Professor (Zoology)
A.J. Davison, Ph.D. (Rutgers, N.J.), Professor (Kinesiology, SFU)
B.P. Dunn, Ph.D. (Brit. Col.), Adjunct Professor (Kinesiology, SFU)
M.P. Rosin, Ph.D. (Toronto), Associate Professor (Kinesiology, SFU)
S.S. Tsang, Ph.D. (Brit. Col.), Assistant Professor (Medical Genetics)
J.R. Vielkind, Ph.D. (Giessen), Assistant Professor (Pathology)

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Dr. B. Palcic, Cancer Imaging Section, BCCRC
Dr. A. Judd, St. Martin's Hospital, La Loche, Sask.
Lung Cancer Research Group, VGH
Occupational Diseases Research Unit, UBC-VGH

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Drs. J.J. Black & A. Maccubbin
Roswell Park Memorial Institute, Buffalo, N.Y.
Dr. H.D. Ochs
University of Washington, Department of Pediatrics, Seattle
Drs. R. Gatti and E. Boder
University of California, Department of Pathology, Los Angeles
Drs. G. Stuart, M. Westerfield & J.A. Weston
University of Oregon, Eugene
Dr. D.C. Morizot
University of Texas Science Park, Smithville
Dr. K.D. Kallman
Osborn Laboratories of Marine Science, Brooklyn, N.Y.

Israel:
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Department of Zoology, Tel Aviv University, Tel Aviv

France:
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International Agency for Research on Cancer, Lyon

The Netherlands:
Dr. R. Baan
Medical Biological Laboratory TNO, Department of Genetic Toxicology, Rijkswijk

Switzerland:
Dr. R. Salkeld
F. Hoffmann-La Roche & Co., Basel

India:
Drs. B. Mathew & M. Krishnan Nair
Regional Cancer Centre, Trivandrum, Kerala

Malaysia:
Dr. A. Ong
Palm Oil Research Institute, Kuala Lumpur

Japan:
Drs. H. Kasai & H. Fujiki
National Cancer Centre, Tokyo

Visiting Scientists:
Yin-Juan Xie, M.D.
Dalian Medical College, Dalian, People's Republic of China
Dr. Katja Breskvar
Faculty of Medicine
E. Kardelj
University of Ljubljana, Ljubljana, Yugoslavia

POSTDOCTORAL FELLOW

B. Sadaghiani, Ph.D.

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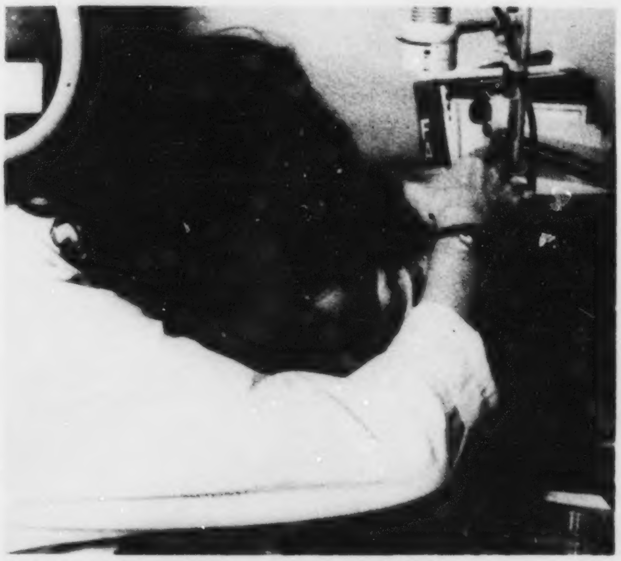
Linda Cameron M.Sc., Pathology
Michelle Chan, M.Sc., Kinesiology
Samuel Chong, M.Sc., Zoology
Dolores Fatur, M.Sc., Kinesiology
Ann-Marie Gilbert, M.Sc., Kinesiology
Paul Hornby, Ph.D., Pathology
Wan-Fung Kwan, M.D., Ph.D., Pathology
Ronald Lauener, M.Sc., Genetics
Gang Li, Ph.D., Zoology
Kathleen McKnight, M.Sc., Kinesiology
Jim Moon, Ph.D., Kinesiology
Eunice Rousseau, M.Sc., Kinesiology
Don Steele, M.Sc., Kinesiology
Xeufeng Yin, M.Sc., Kinesiology
Qiao Zhi, M.Sc., Kinesiology



Dr. Miriam Rosin examines tissue culture samples of fibroblasts from individuals with genetic syndromes predisposing to cancer.

RESEARCH PROJECTS

I. CHEMOPREVENTIVE TRIALS ON ORAL CANCER WITH BETA-CAROTENE AND VITAMIN A

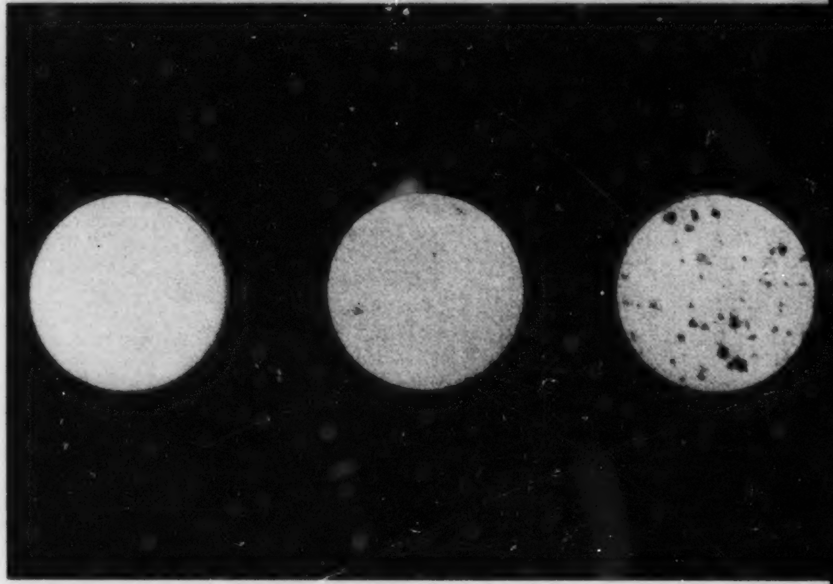
Drs. Hans F. Stich, A. Paul Hornby, Siu Sing Tsang and Gang Li, Environmental Carcinogenesis Unit, B.C. Cancer Research Centre; Drs. M. Krishnan Nair and Babu Mathew, Regional Cancer Centre, Trivandrum, India; and Drs. A. Ong, O. Keat and C. Hin, Palm Oil Research Institute, Kuala Lumpur, Malaysia

Objectives

Oral cancer is responsible for a large fraction of cancer mortality among Indian chewers of tobacco-containing betel quids and among American and European snuff dippers. Since patients with oral cancer have low levels of plasma vitamin A, or consume a diet low in vitamin A or vitamin A precursors such as beta-carotene, the question has been repeatedly raised whether supplementation of the diet with chemopreventive agents can reduce the risk of developing oral cancer.

Remission of Oral Leukoplakias and Inhibition of the Development of New Leukoplakias

The participants in the intervention trial were fishermen of Kerala (India), in the vicinity of Trivandrum, who chewed an average of 17 betel quids daily. The betel quids were



Enhancement of bovine papillomavirus (BPV) DNA-induced cell transformation by a tumour promoter, Mezerein. From left to right: untreated mouse fibroblasts; mouse fibroblasts transfected with BPV DNA; mouse fibroblasts transfected with BPV DNA and grown in the presence of Mezerein (0.3 ng/ml).

A selection of some commercially available brands of oral and nasal snuff. None of these packages carries any kind of health warning.

composed of tobacco, areca nut pieces, slaked lime and betel leaf. The chewers were distributed at random into four groups: I, placebo capsules; II, beta-carotene (180 mg/week); III, beta-carotene (180mg/week) plus vitamin A (100,000 IU/week); and IV, vitamin A (200,000 IU/week). The participants continued to chew in their accustomed manner during the entire period of the trial. These pilot trials on tobacco/betel quid chewers revealed that vitamin A treatment induced the remission of oral leukoplakias in 57.1% of participants (n=21), and that vitamin A plus beta-carotene administration resulted in remission in 27.5% (n=51). Both treatments completely inhibited the appearance of new leukoplakias during the 12-month trial period. Beta-carotene administration had a lesser effect on established precancerous oral lesions, but prevented the development of new ones.

Erika Cheng, recipient of a B.C. Cancer Studentship, extracts DNA for determining the effects of tumour promoters on cellular levels of BPV DNA.

Maintenance of a Chemopreventive Effect Over Prolonged Time Periods with Low Maintenance Doses

We focused our attention on the maintenance of a protective effect once the administration of the chemopreventive agents had been terminated. Currently, there is a dilemma, in that prolonged administration of vitamin A or synthetic retinoids may cause undesirable side-effects, and that withdrawal of treatment may lead to the recurrence of the preneoplastic lesions. To cope with this situation, we are currently conducting a series of "maintenance" trials. The original 6-month administration of vitamin A (200,000 IU/week) is being followed by treatment with non-toxic doses of vitamin A (50,000 IU/week) and beta-carotene at doses ranging from 60 to 12 mg/week. This study is based on the idea that the remission of leukoplakia requires heavy chemotherapeutic doses, whereas lower chemopreventive doses may suffice to prevent the development of new lesions or the recurrence of the original ones.

Maintenance of a Chemopreventive Effect Over Prolonged Time Periods with Food Products Rich in Beta-carotene

Considering the approximately 400 million betel quid chewers, the 100 million users of various tobacco/slaked lime mixtures, and the 30 million American and European snuff dippers, the prolonged administration of beta-carotene or retinoid capsules does not appear to be economically acceptable. The logistics of distribution would be staggering. We will attempt to resolve this issue by the administration of red palm oil as a cheap source of beta-carotene. In its crude form, it contains between 0.7 and 1.6 mg/ml beta-carotene, and 0.6 to 1.0 mg/ml tocopherol and tocotrienols, some of which are good electron scavengers, and have antimutagenic and anticarcinogenic activity. Two sets of experiments are currently underway to see whether red palm oil could induce the remission of oral leukoplakia, or could at least be used to maintain a chemopreventive effect already obtained using higher doses of vitamin A or synthetic retinoids.

II. MECHANISM OF RETINOID ACTION

Drs. Siu Sing Tsang, Hans F. Stich and Gang Li

Recently, human papillomaviruses have been found to be associated with human precancerous lesions or cancers, including oral lesions. The question has been raised whether retinoids or beta-carotene exert their protective effect through interference with the replication or expression of papillomaviruses. We used bovine papillomavirus (BPV) DNA as a model system, cultured mouse cells (C127) as a target, and the formation of colonies of neoplastically transformed cells as an endpoint. The action of retinoic acid was tested by adding the chemopreventive agent at different time intervals after BPV DNA transfection, and estimating the number of neoplastically transformed colonies. Complete inhibition was observed when cells were continuously exposed after transfection to retinoic acid at doses ranging from 0.5 to 1 x 10^{-5}M. Unfortunately, the inhibitory effect of a short

Research Assistant Barbara Schmidt weighs X-gal in preparation for an experiment to identify transformed cells.

(14 days) treatment with retinoic acid was reversible. Transformed foci started to form after withdrawal of retinoic acid. However, the number of BPV DNA copies gradually decreased when the cells were grown over several generations in the presence of retinoic acid (5 x 10^{-6}M). After approximately 30 cell generations, the cell cultures appeared to have less than one copy of BPV DNA, finally reaching undetectable levels. Similarly, a complete loss of BPV DNA copies from transformed cells and a reversal of transformed properties was obtained by prolonged treatment with interferon (studies by other investigators). It is of interest to note that the reduction of BPV DNA copies in cells exposed to retinoic acid starts earlier and progresses more quickly, as compared to the cell cultures treated with interferon. Once the viral DNA has been lost from the cells due to retinoic acid treatment, the cells also lose their neoplastic behaviour. Only in such a situation can one speak of a "cure". The next step of this project will focus on the extent to which the studies on cultured cells can be transferred to human subjects.

III. MODULATION OF BOVINE PAPILLOMAVIRUS DNA-INDUCED CELLULAR TRANSFORMATION BY TUMOUR PROMOTERS

Dr. Siu Sing Tsang

Tumour promoters are chemicals that enhance the frequency of tumour formation in animals previously exposed to carcinogens. They are either synthetic or can occur naturally. They have been implicated as causative agents of diarrhetic food poisoning as a result of shellfish consumption and swimmer's itch. Several tumour promoters, such as a phorbol ester from croton oil, teleocidin A-1 from *Streptomyces* (kindly provided to us by Dr. H. Fujiki and Dr. T. Sugimura of the National Cancer Center, Tokyo, Japan), and Mezerein (an antileukemic agent), from the plant *Daphne mezereum*, have been found to enhance the frequency of cell transformation induced by bovine papillomavirus DNA. The bovine papillomavirus DNA-mouse cell transformation system may be useful in the screening of chemopreventive agents and tumour promoters. In order to better understand the molecular mechanism underlying the effects of chemopreventive agents and tumour promoters, we plan to identify the genes regulated by these chemicals using molecular cloning techniques.

IV. MEASUREMENT OF GENETIC DAMAGE FROM ENVIRONMENTAL CARCINOGENS

Dr. Bruce P. Dunn

Most environmental carcinogens (cancer-causing agents) are believed to act by binding to and damaging DNA, which is the genetic material of cells. We have developed and validated new methodology for increasing the sensitivity of detecting this type of genetic damage. The new methods use high pressure liquid chromatography and thin-layer chromatography to isolate damaged DNA subunits, and a "postlabelling" procedure

Research Assistant Dorothy Hwang explains the preparation of tissue culture medium to Darlene Redenbach, a Ph.D. student in the Department of Anatomy, U.B.C.

Gang Li, a Ph.D. student from China, performs CDNA cloning of retinoic acid regulator gene sequences.

for measuring them. We have used these methods to show genetic damage in wild fish living in contaminated waterways, and which suffer from cancer related to pollution. Recently, we have examined the possibility of detecting genetic damage in the DNA of small lung biopsies from patients undergoing diagnostic bronchoscopy. Smokers showed high levels of genetic damage, indicating DNA binding of chemicals from cigarette smoke. This damage was not present in DNA in white blood cells from the same patients, consistent with the lung being the major site of cancer in cigarette smokers. The procedures that we have developed represent an exciting new approach to investigating the mechanisms by which smoking causes cancer.

V. DEVELOPMENT OF NEW APPROACHES TO IDENTIFY INDIVIDUALS GENETICALLY PREDISPOSED TO CANCER

Dr. Miriam P. Rosin

Although genetic factors have long been implicated in the overall risk for cancer, our knowledge of these factors is still somewhat limited. A prime reason for the paucity of information on this subject stems from our inability to identify such individuals. The research focuses on a group of individuals belonging to the genetic syndrome, ataxia-telangiectasia (A-T). Parents of A-T patients are clinically unidentifiable, yet they are believed to comprise 2.8% of the general population and to represent 5% of all persons dying from cancer before the age of 45, and up to 15% of all breast cancers. These parents of A-T patients carry only a single defective A-T gene, with two genes being essential for development of the syndrome. Currently, the parents are identified only after the birth of a child with A-T. Both parents have to carry the defective gene and to pass it on to the child. The research has two aims: first, to develop new approaches to identify the carriers of A-T, since they could represent a significant fraction of individuals at high risk for cancer; and second, to develop an understanding of how this genetic defect leads to an enhanced cancer risk.

VI. ROLE OF ACTIVE OXYGEN IN CELLULAR GENOTOXICITY

Dr. Allan J. Davison

The group at Simon Fraser University continues to unravel the role of free radicals in damage to the genetic material. Oxygen radicals are almost always involved in the cell changes which lead to the appearance of a cancer (tumour promotion). The group has shown that a "pro-oxidant" (6-hydroxydopamine) which, in the presence of oxygen, produces cell-damaging free radicals, causes cellular mutations in the Ames test, and damages chromosomes in cultured mammalian cells. Enzymes which remove free radicals (such as superoxide dismutase or catalase) were protective, as were metal binding agents (like EDTA or desferrioxamine). Metal ions (iron, copper, aluminium, manganese or vanadium) act as amplifiers, greatly increasing the damage caused by pro-oxidants. Anti-oxidants protect against such damage, either by binding metals, or by "scavenging" free radicals, and breaking the chains which by branching magnify the genetic damage. Three new graduate students have the task of determining which anti-oxidants are most effective, and whether the protective action of beta-carotene is due to its anti-oxidant effects. If an assay of anti-oxidant activity can be developed which parallels the anti-cancer actions of chemopreventive agents, it will be possible to test new agents and new combinations of agents within hours instead of the months now required to obtain the same information from clinical trials.

VII. THE SIGNIFICANCE OF TUMOUR SUPPRESSOR AND OTHER CANCER GENES IN THE GENESIS OF TUMOURS

Dr. Juergen R. Vielkind

Since the middle of the last century, it has been known that certain cancers cluster in families, suggesting that cancer is a genetic disorder and that cancer predisposition is an inherited trait. Recently, it has been shown that this predisposition is frequently due to an inherited defective (recessively mutated) autosomal tumour suppressor gene, and that a tumour also develops after the other copy of the gene has been mutated. A large variety of human tumours, such as retinoblastoma and osteosarcoma, Wilms' tumour, rhabdomyosarcoma, hepatoblastoma, adrenal carcinoma, bladder carcinoma, renal cell carcinoma, ductal breast carcinoma, colon carcinoma, meningioma, acoustic neuroma, pheochromocytoma, and glioblastoma, follow this mode of tumorigenesis. The normal function of tumour suppressor genes is unclear at this time.

To date there is only one vertebrate animal tumour model in which to follow the genetics of such predispositions, and to analyze the significance of genetic changes in the genesis of cancer: the heritable melanoma formation in small tropical fish known as platyfish and swordtail. In particular, the case emulates a certain form of familial human melanoma. In cooperation with Drs. D.C. Morizot (University of Texas) and K.D. Kallman (Osborn Laboratories, New York), we had already recognized a melanoma suppressor gene, and suggested that changes in such tumour suppressor genes may have a general significance for human tumour formation. More recently, we have been able to exactly localize this gene, and demonstrated that a different, sex-linked gene is crucial as to whether or not a melanoma can form regardless of the recessive mutations in both melanoma suppressor genes. Interestingly, this sex-linked gene can cause melanomas in a dominant fashion if mutated. Although several researchers have suggested a cooperative effect between tumour suppressor genes and other, oncogenic genes, this is the first case in which such a direct relationship has been demonstrated. Experiments are underway to molecularly clone the melanoma genes. In order to analyze the biological function of the cloned genes, we have developed gene transfer systems in which the regulated expression of these genes can be studied. In cooperation with researchers from the Terry Fox Laboratory, and from the Universities of Oregon, Eugene, and Tel Aviv, Israel, we are optimizing these systems. Very recently, we obtained evidence that the mutation in the sex-linked gene leading to melanomas causes the pigment cell precursors to develop earlier than the normal ones, and we also have evidence that the gene codes for a transmembrane protein. We speculate that the mutation-caused change in this protein triggers mistiming in pigment cell development, and is one factor in tumour formation.

The research staff involved in these studies include postdoctoral fellow, Dr. Bahram Sadaghiani, research assistants, Barbara Schmidt, Arlene Sullivan and Bruce Woolcock, and graduate student Samuel Chong. Our fish are cared for by Doreen Low. We gratefully acknowledge support from the B.C. Cancer Foundation, Medical Research Council of Canada, and the National Institutes of Health (USA).

Dr. Bruce Dunn selects specimens of frozen fish tissue for analysis of genetic damage caused by environmental carcinogens.

Terry Fox Laboratory

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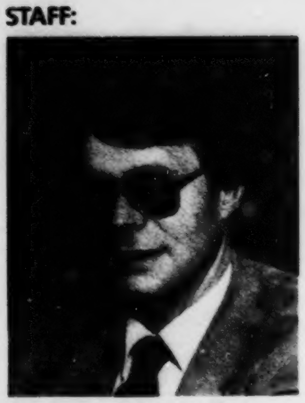

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Overview

The primary goal of the research undertaken in the Terry Fox Laboratory is to improve the diagnosis and treatment of leukemia and related types of cancer. To achieve this, a multi-disciplinary group of laboratory cancer researchers and physicians has been brought together under one administrative structure. Thus advances made in the laboratory can be moved quickly into the clinic. Conversely, patient blood and marrow specimens needed for laboratory research are readily available. The net result is that progress in both the clinic and in the laboratory can be made more rapidly.

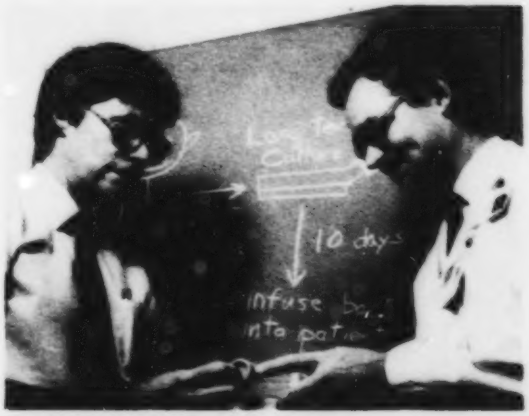
Probably the most spectacular advance in the last year has been the promising first clinical application of a new approach to the treatment of chronic myelogenous leukemia based on a discovery made in the Terry Fox Laboratory in 1982. The discovery was that under certain tissue culture conditions that stimulate the growth of normal blood cells, leukemic cells die. Thus incubation of marrow cells from patients with leukemia under appropriate conditions provides a method for the selective removal of leukemic cells, thereby making possible the use of such incubated marrow for autologous bone marrow transplantation.

Other advances have been made in understanding the regulation of normal and leukemic cell growth, in the development of methods for making specific changes in the genetic make-up of human blood-forming cells and in analyzing how to generate cells that may help fight against cancer within the body. A more detailed description of current areas of activity and scientific achievements during the last year is provided in the latter sections of this report.

A major part of the funding for the research done by the more than 80 people now working in the Terry Fox Laboratory comes from a prestigious 5 year Group grant from the National Cancer Institute of Canada. In addition significant support has also been received from the Medical Research Council of Canada, the British Columbia Health Care Research Foundation, the British Columbia Medical Services Foundation (administered through the Vancouver Foundation), the Cancer Research Society and from Behring Company.

We are particularly proud of the Medical Research Council Scholarship awarded this past year to Dr. Dixie Mager. This will provide most of the funds for her salary for the next five years. Other senior staff who hold similar competitive career awards from national agencies are Dr. Connie Eaves (who is a Terry Fox Research Scientist of the National Cancer Institute), Dr. Gerry Krystal (who holds a Senior Research Scientist Award from the National Cancer Institute), and Dr. Keith Humphries (who is a Scholar of the Medical Research Council). Salary support for the other Senior Staff is provided by the Cancer Control Agency of British Columbia, Vancouver General Hospital, BC Children's Hospital and University of British Columbia. A large and important group in terms of research productivity are the 33 postdoctoral fellows, graduate students, and summer students who have worked on projects in the Terry Fox Laboratory during the last year. Seventeen of these individuals have also obtained their own full-time salary support in the form of competitive independent awards from outside agencies, including the National Cancer Institute, Medical Research Council, National Science and Engineering Research Council, University of British Columbia and L'Association pour la Recherche contre le Cancer (France).

Teaching is also a vital part of cancer research, especially in view of recent governmental reports projecting an increasing number of cancer patients and an insufficient number of trained biomedical investigators in



Dr. Allen Eaves, Director of the Terry Fox Laboratory and Head of Hematology at the Vancouver General Hospital and Cancer Control Agency talks about long-term culture purging to Dr. Michael Barnett, a Hematologist and member of the Leukemia/BMT Program. This method of removing leukemic cells from normal stem cells for the purposes of autologous bone marrow transplantation in patients with chronic myelogenous leukemia was developed in the Terry Fox Laboratory and is now being tested in patients treated at the Cancer Control Agency of British Columbia and the Vancouver General Hospital.

the near future. Most graduate students in the Terry Fox Laboratory are enrolled either in the Genetics Program, the Experimental Pathology Program or the Department of Microbiology of the University of British Columbia. The Senior Staff of the Terry Fox Laboratory has organized, with the assistance of other staff in the BC Cancer Research Centre, a joint graduate and undergraduate level course called "Oncogenetics". This course has been offered at the University of British Columbia for several years and provides an important liaison between the student body on campus and the Centre. Dr. Dixie Mager now serves as the Co-ordinator for this very popular series of lectures which provide an introductory review of a variety of topics in the rapidly evolving field of cancer cell biology and genetics. Within the Terry Fox Laboratory a number of university-accredited seminar courses are also offered. These include a literature review course (Journal Club) and Work-In-Progress (WIP) series. In addition a 20 lecture course on the use of computers, word processing, statistical analysis and data management was taught again last year by Mr. Don Henkelman, Statistician and Systems Analyst in the Terry Fox Laboratory.

An important development has been the final acquisition of sufficient funds to allow construction to begin on the long awaited Level III/Gene Therapy Facility. Most of the funding for this facility is being provided by generous donations from Mr. Joseph Cohen, the Mr. and Mrs. P.A. Woodward Foundation and the Order of the Eastern Star. Additional funds have been provided by the Faculty of Medicine and the Faculty of Graduate Studies of the University of British Columbia and the BC Cancer Foundation. Planning of this laboratory is complete and space adjacent to the Terry Fox Laboratory has been allocated. The facility has been carefully designed to provide the desired level of containment for genetically engineering human cells in the laboratory. The first generation of vectors to enable this work to proceed are currently being constructed in the Terry Fox Laboratory. These vectors will permit a precise evaluation of the function of specific regulatory elements encoded by certain human genes and the value and feasibility of modifying the genetic make-up of human cells using retroviral vectors. The new laboratory will also provide expanded facilities for laboratory manipulation of marrow transplants including gene therapy protocols being planned in conjunction with the Bone Marrow Transplant Program under the direction of Dr. Gordon Phillips. Funds to equip the facility are currently being sought.

Over the last year a number of other projects have been undertaken. Income from the Media Preparation Service was used to complete construction of the Molecular Oncology Laboratory which accommodates the research of Dr. Donna Hogge and to improve the water purification system of the Terry Fox Laboratory. These funds also made possible the purchase of desks and bookshelves for our rapidly expanding numbers of trainees in a year where core support for the purchase of furniture has been highly restricted.

In September, 1987 after several months of careful planning, the Division of Hematology including the staff of the Terry Fox Laboratory hosted a very successful international conference on "Stem Cells and Autologous Bone Marrow Transplantation". This conference was funded primarily by a grant from the National Cancer Institute and thus became the 4th Terry Fox Cancer Conference. By the start of the conference registration had reached an unanticipated 210 people. Twenty-seven presentations from world experts from the United States, Europe and Australia as well as Canada provoked extensive discussion and facilitated the exchange of a great deal of new information. The Conference clearly fostered recognition of Vancouver as a leading bone marrow transplant centre and demonstrated the importance of hosting such conferences which bring clinicians and laboratory scientists with common interests together. The success of the 4th Terry Fox Cancer Conference is also a tribute to the dedication and hard work of the secretarial and administrative staff of the Terry Fox Laboratory who played a key role in making it happen.

The Senior Staff have had a busy and productive year in terms of invited lectures, publications and attendance at a large number of national and international meetings, in many instances as invited speakers. Many of the Senior Staff also serve on peer-review grants panels including those of the National Cancer Institute, the Medical Research Council, and the Canadian Red Cross, as well as the National Institutes of Health (NIH) in the United States. Several of the Senior Staff are also Associate Editors or members of editorial boards of various international journals.

Characterization and Regulation of Primitive Blood-Forming Cells

C. Eaves

The most primitive blood cell precursors in the bone marrow are pluripotent — that is they can give rise to all of the many different mature cell types found in the blood (white cells that fight infection, red cells that carry oxygen, platelets which help make the blood clot). These stem cells also have a very extensive growth and self-replicative capacity, sufficient in fact for a single stem cell to repopulate the entire blood-forming and immune system of an individual. Most of these very primitive stem cells reside in the bone marrow in a resting (non-dividing) state. Normally they are recruited to divide and produce new blood cells at a very slow rate since each one can produce billions of daughter cells. However, when a crisis occurs requiring large numbers of blood cells to be produced rapidly, such as during a period of severe infection or injury leading to extensive blood loss, more stem cells are recruited and stimulated to address this need for new blood cells. Unfortunately, one of these stem cells occasionally suffers genetic damage that results in an uncontrolled activation of its awesome proliferative potential. The resulting over-production of cells can lead to a spectrum of different cancers of the blood-forming system, including: all of the different kinds of leukemia, lymphoma, Hodgkin's disease, multiple myeloma, polycythemia vera, and essential thrombocytosis.

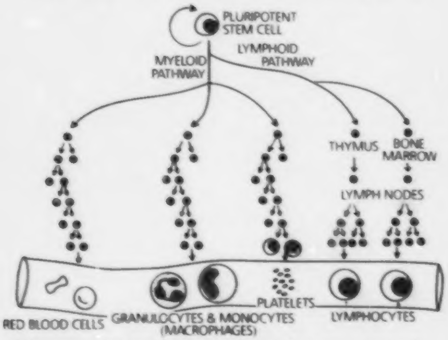


Diagram of how blood cell production occurs by a process involving many divisions of a primitive "stem" cell, whose daughter cells develop later into all of the different types of cells found in the blood. Much of the research in the Terry Fox Laboratory is devoted to obtaining a better understanding of this important cell type, how it is normally regulated, and how it can change to give rise to different types of blood cancer.

Over the last 15 years, this laboratory has played a pioneering role in the development of tissue culture methods designed to study the behaviour and regulation of primitive blood stem cells. The research interests of Dr. C. Eaves are focused on the identification of conditions required to support the growth and differentiation of various types of primitive blood-forming cells. Such studies serve as an important starting point to identify more precisely the cell types and molecular interactions involved in the regulation of primitive blood-forming cells and how these may be overcome or circumvented to allow the development of leukemia and related cancers of the blood.

Dr. Teru Otsuka, a Hematologist and Postdoctoral Fellow from Japan, consults with Dr. Brigitte Swolin, a Hematopathologist and Cytogeneticist on sabbatical from Sweden, on the scoring of blood cell colonies. Many of the cells that give rise to the various types of mature blood cells can only be identified by their ability to grow and form colonies of cells in semi-solid culture media. The resulting colonies are then scored and provide a measure of the number of types of stem cells in patients with leukemia.

It is thought that the production of most blood cell types in the bone marrow is controlled locally by a network of "stroma" (supporting) cells. These cells represent the framework of the marrow tissue and make up the blood vessels and synthesize cartilage and bone. It appears that at least some of these marrow stromal cells also have the capacity to respond to signals from activated or injured white blood cells by producing factors that can stimulate the growth of adjacent "sleeping" primitive blood-forming cells. These events have been reproduced in long-term marrow cultures in which both stromal cells and primitive blood-forming cells are maintained and their interactions with each other allow blood formation to proceed in culture for extensive periods of time. By manipulating these cultures in defined ways and by isolating and analyzing the role of each of the component cell types, we are beginning to understand how normal blood cell production is controlled in the marrow and how complex this control process is.

Analysis of what goes on in long-term marrow cultures has also provided new insights into the hierarchy of primitive blood-forming cells that exist in the marrow. Recent studies indicate that the cells that initiate blood formation in these cultures under the control of marrow stromal cells may correspond to the cells that are able to permanently repopulate the blood-forming system after transplantation. Comparisons of the repopulating potential of single genetically marked cells both after transplantation and in long-term marrow culture will help to clarify what properties cells with different potentialities have. Studies from several centres have shown that a single mouse marrow cell can repopulate and maintain the entire blood-forming system of a transplanted recipient mouse for many weeks. Recently analysis of a series of transplant patients in the Vancouver program has shown that the same thing can be seen in humans. This observation provides the first direct documentation that adult human marrow contains a cell type that can regenerate the immune system as well as the other blood cell types produced in the marrow.

Dr. Connie Eaves, Deputy Director of the Terry Fox Laboratory and Leader of the National Cancer Institute funded Group Program, hears the results of B cell separation experiments performed by Dr. Peter deVries, a Postdoctoral Fellow from The Netherlands.

Experiments to study how the precursors of antibody-forming cells (pre-B cells) develop in the marrow have also been undertaken. These studies have identified a new growth factor specific for pre-B cells. They have also provided evidence that pre-B cell cancers (i.e. acute lymphoid leukemia) may be due to the abnormal acquisition by pre-B cells of the ability to produce their own growth factor.

Cell Separation and Analysis

P. Lansdorp

The identification and isolation of cells with a particular functional property or unique cell surface characteristic is an important approach to understanding the regulation of cell growth at all levels in the hemopoietic and immune systems. Monoclonal antibodies are particularly useful in this regard because of their exquisite specificity. Dr. Lansdorp has developed a procedure for generating complexes of 4 monoclonal antibody molecules which have ideal cross-linking properties. These "tetramers" are being evaluated for their ability to target drugs, isotopes and genes to selected cells. The tetramer methodology itself is also being further improved. New hybrid monoclonal antibodies have been developed to provide purer reagents. These are being used to develop simple procedures for allowing rare cell types in a mixed population of cells to be attached via a small molecular weight hapten to glass beads and then specifically detached.

This cell separation strategy is being used to isolate and characterize the most primitive blood-forming cell types. These cells are thought to constitute less than 0.01% (1/10,000) of the marrow. Thus their purification is a formidable task. The development of a procedure suitable for clinical scale-up requires that a relatively simple series of rapid, non-toxic and highly specific separation steps be defined. Preliminary studies with mouse marrow suggest that the

Dr. Peter Lansdorp discusses the use of the cell washer with members of his team in the Cryogenic Laboratory. This machine can separate large volumes of white cells away from red cells and is the first step in preparing a marrow harvest for autologous transplantation. Left to right: Mrs. Sara Abraham, cryogenic technologist, Dr. Heather Sutherland a hematologist and Terry Fox Physician Scientist Fellow working towards a Ph.D., and Dr. Terry Thomas a Post-doctoral Fellow.

use of tetramers will allow many of these requirements to be met and will permit an extremely high purification of viable repopulating cells to be rapidly attained. Experiments with human marrow to establish appropriate conditions for clinical studies have also been initiated and a method for achieving significant enrichment of the desired cells has already been developed.

This technique of cell separation on columns of glass beads is also being developed for applications where the goal is to deplete bone marrow cell suspensions of specific subpopulations of unwanted cells. An immediate application of this methodology is to reduce the number of T-lymphocytes in marrow being prepared for transplantation. This may help to reduce the severity of graft-versus-host disease which is a common serious complication of bone marrow transplantation.

Regulation of T-Lymphocyte Proliferation

F. Takei

Lymphocytes play essential roles in the body's natural defense against infectious disease and possibly against cancer. Lymphocytes also produce many hormone-like factors that influence the growth and function of other cell types including cells of the blood-forming system. The lymphocytes that are normally circulating in the blood and the lymph are resting, functionally inert cells. Only after they encounter foreign materials such as invading microorganisms do they become activated and begin to proliferate and display important functions. One of the research interests of Dr. Takei's laboratory is to find out exactly how resting lymphocytes become activated, what interactions with other cells take place, how these are effected and what changes take place on the surface of the lymphocyte to facilitate this activation.

Dr. Fumio Takei discusses lymphocyte function with three of his students: Carmine Carpenito (recipient of an MRC Studentship), Kathleen Horley (recipient of an NSERC Studentship), and Po-Ying Chan (recipient of an MRC Studentship). Dr. Takei's group has discovered, purified and partially sequenced two cell surface proteins important in lymphocyte activation.

Dr. Takei's group has discovered two molecules that are on the surface of activated lymphocytes and appear to be involved in this activation process. The two proteins have been purified and their structure partially determined. Based on the information obtained, it has been possible to isolate (clone) the two genes encoding these proteins. Further analysis of one of these genes showed that the product, i.e. the cell surface protein, may be a molecule that helps to allow lymphocytes to interact with cells that present antigens to lymphocytes. Ongoing research will further characterize the function of this cell surface protein on activated lymphocytes. Such information will be important in the development of methods for manipulating immune responses so that desirable immunity, such as anti-cancer immunity, can be boosted while unwanted immunity such as auto-immunity or graft-versus-host responses can be inhibited.

Analysis of Immunodeficiency in Marrow Transplant Recipients

(H. Klingemann)

Immunodeficiency and relapse of the underlying malignant disease remain the two major obstacles to further improving survival and quality of life after therapy involving bone marrow transplantation. The effects of hemopoietic growth factors on white blood cell functions are being studied in vitro to learn how to improve immunocompetence in these patients. This involves assessment of various functions of T-lymphocytes, B-lymphocytes, and monocytes at various times after marrow infusion to see whether and when such cells are able to respond to these stimuli. To improve the recovery of blood cell production and the immune competence of the transplant patient, a clinical trial to test the effect of GM-CSF administration is being initiated by the Bone Marrow Transplant team. GM-CSF is one of the hemopoietic growth factors to which monocytes, granulocytes and their precursors show a very marked response. Analysis of cells from marrow transplant patients receiving GM-CSF by comparison to control patients will also provide a unique opportunity to evaluate the in vivo effects of GM-CSF on a variety of cell types whose functional status can be measured in the laboratory.

BLOOD
Cell
Experimental Hematology

Dr. Hans Klingemann, hematologist and member of the Leukemia/BMT Program hears about a new finding from Dr. Fred Kohn, a Ph.D. in pharmacology and Postdoctoral Fellow working in the laboratory on methods of how to improve the immune capability of bone marrow transplant recipients.

Dr. Klingemann's group is also investigating the role of fibronectin in modulating immune responses. Fibronectin is a ubiquitous constituent of the extracellular matrix, the material found between cells. It can influence a variety of monocyte functions, including phagocytosis and their production of certain "monokines". Monokines are molecules released by activated monocytes that can stimulate other blood cell types. Examples are interleukin-1 and tumour necrosis factor. One project is directed at determining how fibronectin stimulates monokine release by monocytes. Dr. Klingemann has shown that fibronectin can enhance the response of stimulated lymphocytes including the weakly responsive lymphocytes characteristic of immune deficient marrow transplant patients. This effect of fibronectin on lymphocytes in tissue culture suggests a novel strategy for improving the immune recovery of marrow transplant patients by the administration of fibronectin. To pursue this possibility, further information about how fibronectin exerts its effects on monocytes is being obtained.

Growth Factors and their Receptors

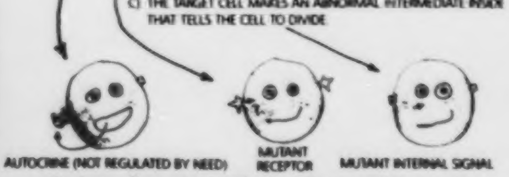
G. Krystal

Mature blood cells (i.e. red blood cells, platelets and white blood cells) have finite life spans in the blood stream and are constantly dying and therefore have to be continuously replaced. The control of normal blood cell production is mediated by both stimulatory and inhibitory factors, i.e. factors that stimulate growth and differentiation, as well as factors that return cells to a quiescent or resting state. The levels of these regulatory factors are critical in determining the number of mature cells released each day into the circulatory system. These regulatory molecules act on responsive blood cell progenitors by binding to specific receptor molecules displayed on the cell surface. Part of the control exercised

Dr. Gerald Krystal and Bert Wognum (a trainee from The Netherlands) consider results of a purification of monoclonal antibodies made against a hemopoietic growth factor and isolated using high pressure liquid chromatography.

by regulatory factors is determined by whether or not a particular cell is able to produce the receptor for a specific growth factor. Binding of growth factors to their receptors causes a small but significant change in the conformation of the receptor. This then initiates a series of chemical signals inside the cell that results in an alteration of its behaviour.

Recently, interest in these regulatory factors and their receptors has increased dramatically because of growing evidence that cancers may result from the abnormal proliferation of cells that have become independent of outside stimulation by growth factors. Some cancer cells have developed the ability to make their own "autostimulatory" growth factors. Other types can make abnormal receptors that do not have to bind growth factors in order to be "turned on", or they may inappropriately produce other molecules inside the cell that maintain a turned on state without receptor activation.


A) THE TARGET CELL MAKES ITS OWN GROWTH FACTOR (AUTOCRINE PRODUCTION)
B) THE TARGET CELL MAKES AN ABNORMAL RECEPTOR THAT TELLS THE CELL TO DIVIDE IN THE ABSENCE OF A GROWTH FACTOR
C) THE TARGET CELL MAKES AN ABNORMAL INTERMEDIATE INSIDE THAT TELLS THE CELL TO DIVIDE
AUTOCRINE (NOT REGULATED BY NEED)
MUTANT RECEPTOR
MUTANT INTERNAL SIGNAL

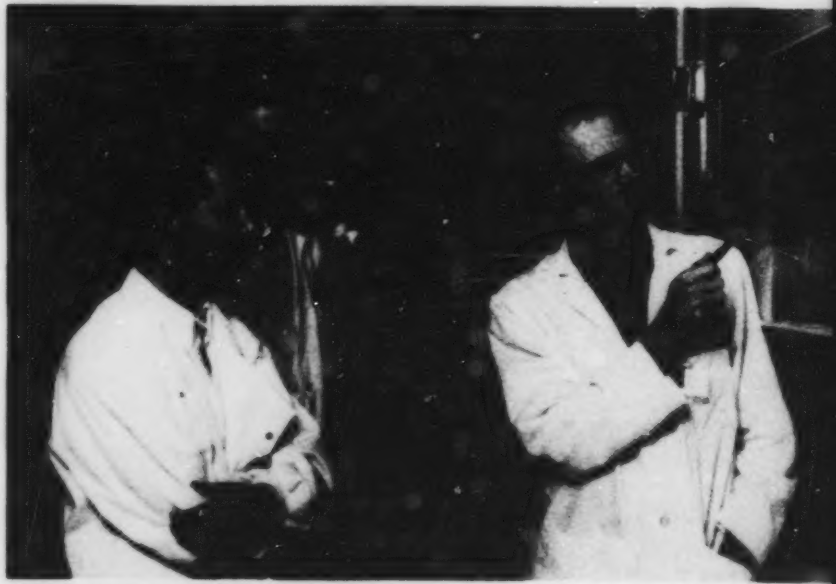
Cartoon illustrating different abnormalities a cell may develop, all of which give the same result: a cell able to divide uncontrollably, the hallmark of a cancer cell.

Dr. Krystal's group is involved in studies of several hemopoietic growth factors to elucidate how these factors regulate cell division and differentiation at the molecular level. A major challenge has been the development of methods to isolate and characterize the cellular receptors for two factors: erythropoietin and interleukin-3. Information about the structure of these molecules and how they interact with the metabolic machinery inside blood-forming cells should prove useful in designing future diagnostic tests and treatment strategies.

Genetic Determinants of Normal and Leukemic Blood Cell Behaviour

K. Humphries

Studies in Dr. Humphries' laboratory are concerned with developing a better understanding of the genes that direct the normal and malignant behaviour of primitive blood-forming cells. Three different areas of research are being pursued. The first focuses on genes that direct the



Dr. Keith Humphries discusses a new gene cloning strategy with three Postdoctoral Fellows: Dr. Graeme Dougherty, a molecular immunologist from Britain, Dr. Philip Hughes, a hematologist and Terry Fox Physician Scientist Fellow, and Dr. Rob Kay, a molecular biologist and recipient of an MRC Fellowship. Cloning genes involved in the regulation of cell growth will provide new clues about defective growth regulation in leukemia and other cancers.

production of hemopoietic growth factors in an effort to better define their role in the regulation of blood cell production. Molecular probes are now available in the laboratory for 15 growth factor genes. These are being used to measure the level and regulation of growth factor gene expression using highly sensitive and specific messenger RNA analysis techniques. Progress is being made in identifying which cells are capable of producing growth factors and in elucidating how abnormal growth factor production may lead to the development of leukemia.

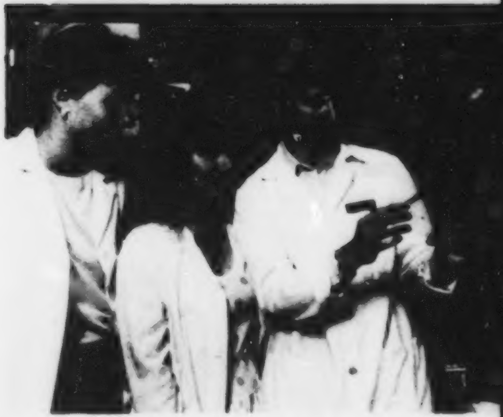
The second major area of research involves the molecular construction of recombinant retroviruses designed to introduce new genetic material into hemopoietic cells. This last year has seen marked improvements in gene transfer efficiencies in the demonstration that gene transfer is possible to the most primitive human blood-forming cell that can be grown in tissue culture. The ability to introduce defined DNA sequences into these primitive blood-forming cells provides a powerful tool for investigating the role that specific genes play in blood production.

Advances have also been made using new strategies for isolating genes important to the function of primitive blood cell precursors A novel gene encoding a component of the cell surface of an immortalized primitive hemopoietic cell line has been isolated. The role this molecule may play in the interaction of primitive blood precursor cells with their changing environment is now being determined. A major effort is also being focused on the isolation of the genes for certain hemopoietic growth factor receptors.

Mobile Genetic Elements in Mutagenesis and Malignancy

D. Mager

The genomes of many species including humans contain large numbers of transposable genetic elements. These elements are sequences in the DNA that have a structure that allows them to move to new locations in the chromosomal DNA at a relatively high frequency. In many lower organisms, rearrangements of these sequences account for a large proportion of new mutations. In mammals, insertions of different types of mobile elements cause mutations by inactivating or activating other genes, including genes that, if altered, may cause cancer (hence the name proto-oncogenes). It is therefore likely that mobile genetic elements contribute to the generation and progression of cancer in humans by altering the expression of genes that normally control cell growth.



Dr. Dixie Mager reviews a Southern blot with Nancy Goodchild, a summer student from the University of Victoria, and Anita Feuchter, a graduate student and recipient of a National Cancer Institute of Canada Studentship. They are studying retroviral-like sequences normally present in the human genome that may play a role in cancer progression.

The research in Dr. Mager's lab is aimed at investigating one type of such transposable elements that is found in human DNA. These elements resemble retroviruses and are thus referred to as endogenous "retrovirus-like" sequences. Efforts are focused on investigating the role of these sequences in normal and malignant growth and development. Dr. Mager has found that members of one family of such sequences are present in approximately 1000 copies in the human genome, including some copies on every human chromosome. Detailed analysis of the genetic structure of this type of element has revealed certain similarities to mouse retroviruses and to an infectious human virus (known as HTLV-1) that causes T-cell leukemia in people. Recent studies indicate that these sequences are expressed at high levels in human embryonal carcinoma cells and at lower levels in several other types of human cells.

The human embryonal carcinoma cells are now being used to investigate factors which alter the expression of these naturally-occurring retrovirus-like sequences and to identify proteins that these elements may encode. Studies are also in progress to identify those regions of the retrovirus-like element that control its transcription. Future experiments will examine the effect of coupling these regulatory sequences to known proto-oncogenes. Studies are also being designed to determine how frequently new rearrangements or insertions of retrovirus-like sequences occur in normal and malignant human cells.

Biology of Human Leukemia

A. Eaves

Cancer of the blood-forming system develops in early cell types called stem cells. Usually only one such stem cell is initially altered (or transformed). This cell then starts to grow unchecked by normal regulatory mechanisms. The diseases that result, including all of the leukemias, differ not only in the patient age group where they are most often seen and the type of therapy to which they are likely to respond, but also in a number of more fundamental biological parameters. These include the type of stem cell initially transformed, the types of proto-oncogenes that are activated or altered, whether or not responses to particular growth regulators are changed, and whether the transformed cells can still develop into mature blood cells or not. In spite of these differences between various types of transformed blood cells, all appear to represent the clonal amplification of single cells and share certain common properties. For example, they suppress the growth and differentiation of residual normal blood-forming cells and the transformed cells, themselves, continue to change, a process referred to as clonal evolution.

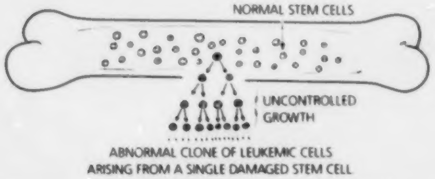

NORMAL STEM CELLS
UNCONTROLLED GROWTH
ABNORMAL CLONE OF LEUKEMIC CELLS ARISING FROM A SINGLE DAMAGED STEM CELL

Diagram illustrating the abnormal amplification of a single transformed stem cell in the bone marrow. This represents the first stage in the development of human blood cancers, such as leukemia.

The research objective of Dr. A. Eaves' current work is to develop tissue culture systems that will allow these features of leukemia to be reproduced, analyzed, and eventually manipulated under defined conditions. At present, leukemic and normal precursors from patients with polycythemia vera, chronic myeloid leukemia, essential thrombocytosis, preleukemia (myelodysplasia) and acute myeloid leukemia are being studied. Evidence of abnormalities in terms of responses to both positive and negative regulators has been obtained. Additional studies using the tools of cellular and molecular biology are being undertaken to establish the generality of these observations in other blood cancers and to determine the basis for the unregulated proliferation observed. Also under investigation is the mechanism of leukemic cell suppression of normal blood-formation using tissue culture methods to reproduce this phenomenon.

Chromosomal Analysis of Normal and Abnormal Cells

D. Kalousek

Chromosomal changes play an integral part in the development of human cancer. In the case of many types of leukemia and lymphoma, a correlation between the properties of the malignant cells and a specific chromosomal abnormality has been recognized. The research interests of Dr. D. Kalousek's laboratory are concerned with determining the stage in the evolution of a leukemic clone at which chromosomal changes occur, the cell type in which these first take place and possible associations with subsequently manifested changes in growth and differentiation.

A significant advance towards these objectives was made with the development in this laboratory of a method for analyzing the chromosomes in cells developing from individual primitive blood cell precursors. The use of this technique to evaluate bone marrow and peripheral blood cells from newly diagnosed, treated and acutely transformed patients with chronic myeloid leukemia and acute leukemia has allowed the demonstration of previously undetectable normal blood cell precursors in many patients.

This procedure is now being used to evaluate new laboratory methods for removing leukemic cells from patients' marrows that can then be used in conjunction with intensified treatment protocols to try and cure the patient's own, otherwise fatal, leukemia. This procedure is also continuing to be used to understand the significance of persisting normal cells to disease progression and prognosis, and to identify suitable patients for treatment with autologous marrow transplants.

Hemopoietic Growth Factor Genes in Marrow Recovery and Human Leukemia

D. Hogge

The nature of the genetic control of normal and malignant blood cell production at the molecular level is an area of current general interest. The genes for a variety of human (and murine) growth factors active on early blood-forming cells have now been cloned, sequenced and expressed in bacterial and yeast hosts. This has allowed the large scale production of highly-purified recombinant proteins. The ready availability of these growth factors in pure form has, in turn, made it possible to define more precisely the effect of various molecules on normal blood cell production, both in tissue culture systems and in animal models.

Dr. Donna Hogge is working with Brigitta Gerhard, a research assistant, on a transfer vector for carrying a human growth factor gene into other cells. This will allow the role of this particular molecule in normal and leukemic cell growth to be evaluated.

Many of these factors are now being tested clinically and are proving of therapeutic value. Aberrant production of hemopoietic growth factors and abnormal responses to these factors have recently been demonstrated in malignant cells from patients suffering from acute leukemia. These latter findings suggest that the abnormal activation of a hemopoietic growth factor gene in a primitive blood-forming cell may play an important role in the development of human leukemia.

The techniques of molecular genetics and cell biology are being used by Dr. D. Hogge to further elucidate how this may occur.

Improving Bone Marrow Transplantation and the Treatment of Acute Leukemia

G. Phillips, D. Reece, M. Barnett and H. Klingemann

The cure of certain leukemias and lymphomas is now feasible using intensive supralethal chemotherapy and radiation therapy in combination with rescue of the marrow by marrow transplantation. This procedure cannot, however, be offered to every patient for a number of reasons. One common limitation is the lack of a suitable brother or sister to serve as the donor of the normal marrow transplant. In order for the donor to be suitable, he or she must be immunologically compatible with the recipient. Otherwise the graft will be rejected by the patient. Alternatively, the graft may grow successfully in the patient but, at the same time, also mount a serious immune reaction against the patient. This is called graft-versus-host disease. Solutions to the basic problems of marrow transplantation lie in developing methods to expand the pool of suitable marrow donors and to control rejection and graft-versus-host disease, and in developing more effective anti-leukemia treatment regimens to reduce the current rate of relapse.

One method of increasing the number of donors is to use partially HLA-matched related donors, HLA-matched but unrelated donors, or to use autologous (the patient's own) bone marrow for transplantation. Each of these strategies requires some laboratory development to establish an adequate procedure for removing unwanted cell populations: T-lymphocytes in allogeneic mismatches, and occult leukemic cells in autologous marrow grafts. Previously used methods have all been found to have unacceptable limitations. The Vancouver program has therefore been concentrating on the development and evaluation of several new approaches. These include new immunophysical strategies for large scale T-cell depletion (allogeneic transplants) and new culture-based, and chemical techniques for the "positive" selection of normal blood cell

Mr. Don Henkelman, statistician and computer systems analyst in charge of Data Management discusses the VAX relational data base for hematology patients with Colleen Evans, data coordinator and Marlene Channell, programmer/analyst. The organization of clinical data for both the Stem Cell Assay Service and the Patient Data Research Program is handled on a computer with terminals throughout the Terry Fox Laboratory and the Division of Hematology in the Vancouver General Hospital.

precursors. Several clinical trials using these strategies are now underway and initial results are promising. A clinical trial to evaluate the role of combined treatment with hemopoietic growth factor infusion (GM-CSF) to enhance marrow recovery will start in the latter part of 1988.

The role of intensive chemotherapy may be viewed as complementary to bone marrow transplantation. All leukemic patients require effective initial chemotherapy to produce remission before bone marrow transplantation. In addition, some patients are at very high risk for transplant-related death, and continued intensive chemotherapy is the preferred treatment in these patients.

Recent experience suggests that nearly 50% of selected acute myelogenous leukemia patients in an initial remission achieve long disease-free survivals with high dose cytarabine. High dose cytarabine-based treatment protocols for patients with acute myelogenous leukemia, chronic myelogenous leukemia in transformation and the myelodysplastic syndromes are therefore being evaluated.

Cancer Endocrinology

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P. W. Gout, Ph.D.

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Honorary Professor (Surgery)

The function of this Section is to evaluate the results of hormonal therapy; to develop new ways of employing hormones, anti-hormones and other factors which regulate the endocrine glands; and to make recommendations concerning the future use of such agents for the management of cancers of the breast, endometrium and prostate.

The Section is engaged in a number of basic and applied investigational projects which include the following studies: mechanism of action of testosterone; control of neoplastic growth by androgens and other hormones; cellular mechanisms of tumour regression; markers of androgen action in human prostate and their potential use in the clinical assessment of prostatic carcinoma; assessment of breast carcinoma for the presence of structurally abnormal receptor genes for estrogen and other hormones; stromal-epithelial interactions in the pathogenesis of benign prostatic hyperplasia; use of anti-androgens in the treatment of advanced prostatic carcinoma; use of 5a-reductase inhibitors in the treatment of prostatic carcinoma; the study of the role of hormones of the anterior pituitary gland in the growth of breast carcinoma and malignant lymphomas; elucidation of the active site of the lactogenic hormone, prolactin; and an investigation of the biological and biochemical changes occurring in malignant lymphomas as they progress from hormonal-dependency to autonomy; and the evaluation of risk of malignancy using flow cytometry and oncogene screening.

Currently, the Section is devoting much of its effort to completing the ground work for the establishment of an Oncogene Detection Service to ensure that the highest quality of cancer diagnosis and treatment continues to be available to cancer patients in British Columbia. There is considerable evidence linking the inappropriate activation of certain normal human genes, termed proto-oncogenes, to the development and spread of cancer. In particular, a strong correlation between the aberrant formation of multiple copies of specific oncogenes (gene amplification) and poor prognosis (ie. a shorter time to relapse and a lower survival rate) has been well documented in neuroblastomas, small cell lung carcinoma, and breast carcinoma. The screening of these cancer-related genes will initially involve measurement of the N-myc oncogene in neuroblastomas, and the c-myc oncogene in breast carcinoma. In addition, it is

Some polypeptide hormones can act as growth factors for cancer cells. Dr. Charles T. Beer, Department of Cancer Endocrinology, is engaged in an analysis of the growth-promoting activities of mutant forms of the pituitary hormone, prolactin, made by recombinant DNA technology.

anticipated that the Oncogene Detection Service will provide an environment that will facilitate the immediate implementation of new prognostic tests in this rapidly developing area.

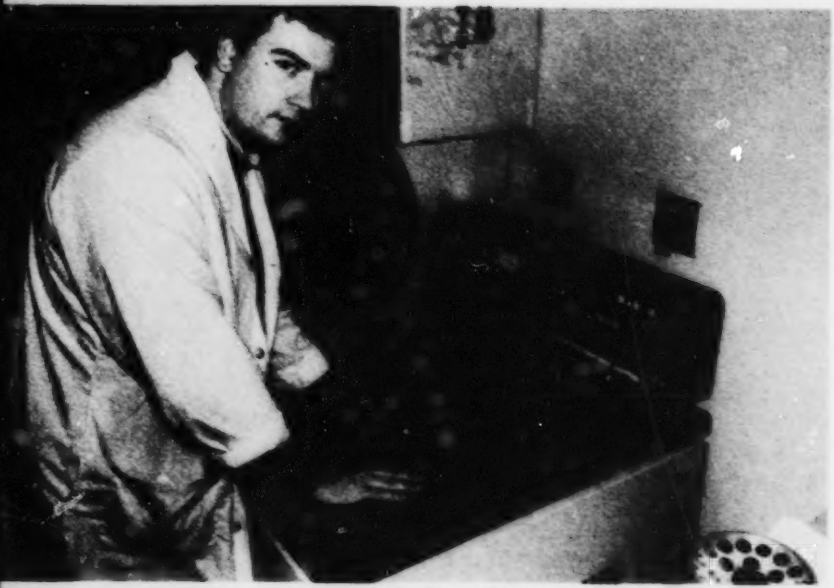
The first clinical application of gene amplification assays has been to measure the copy number of N-myc in neuroblastoma, a rare nerve cell tumour affecting 1 in 125,000 children. The results clearly indicate that the more copies of N-myc present in the cancer cell, the worse the prognosis. In fact, N-myc amplification is a better predictor of survival time than the best clinical data. Accordingly, it is important to identify those children whose tumours have elevated N-myc so that more aggressive treatment can be instituted early enough to affect a cure or to extend their survival.

In contrast to the infrequent occurrence of neuroblastoma, lung carcinoma is the most prevalent form of serious cancer. Furthermore, approximately one quarter of the over 1700 lung cancer cases seen in the Province of British Columbia each year are classified as small cell lung carcinoma, which have the worst prognosis with less than a 10% chance of a cure. Within this group, patients whose tumours are characterized by an amplification of the c-myc oncogene survive only one-half to one-third as long as patients whose tumours do not have extra copies of this gene. Thus with knowledge of the c-myc copy number, the physician can gauge the likelihood of a successful outcome and decide whether the patient should be offered palliative or aggressive therapy.

A third clinical application of oncogene screening is a measurement of the HER-2/neu oncogene in breast cancer. As with lung cancer, breast cancer has a very high incidence of approximately 1400 new patients per year in this province alone and a poor prognosis in cases where the HER-2/neu oncogene is amplified. Recent studies suggest that the HER-2/neu amplification is a better indicator than hormone receptor status, age of patient, and tumour size. High levels of this gene are indicative of a short relapse time and decreased survival. This finding has a major clinical implication in that it may provide a means of selecting those women most likely to benefit from adjuvant chemotherapy after their primary treatment.

Dr. Robert Snoek (Post doctoral Fellow) using fast protein liquid chromatography (FPLC) system to purify and characterize proteins involved in prostatic growth and regulation.

The Section continues to devote much of its effort to the development, testing and application of new drugs which have clinical potential in the treatment of prostatic carcinoma. Owing to demographic changes in the population, the incidence of prostatic carcinoma in the Province of British Columbia will more than double in the next 10-15 years. As long as the cancer remains confined to the prostate it is curable by surgery but in 50-60% of cases it is already spread outside the gland at the time of diagnosis and more complex therapy is necessary to control it and lengthen survival. Investigations conducted by the Section have shown that the effectiveness of the anti-androgen, cyproterone acetate, is enhanced by the co-administration of a small dose of diethylstilbestrol (synthetic female sex hormone) which acts synergistically with cyproterone acetate to suppress the pituitary gland. In clinical testing the combined therapy produced an objective response rate of 98% with survival of 80% of patients after 1 year and 50% after 2 years. Such treatment offers the advantage of a prompt onset of action with a high probability of gaining benefit in terms of symptomatic improvement. In the first Canadian trial of a new long-acting LHRH agonist, ICI 118630, the Section is determining if the incidence of side-effects associated with the use of cyproterone acetate and low-dose diethylstilbestrol can be reduced by substituting ICI 118630 for diethylstilbestrol in



Dr. Simon Freeman recipient of an NCI Fellowship is using various centrifugal steps to purify prostatic nuclear extracts for assay of steroid receptor proteins. The aim of these studies is to identify and characterize the autophagic mechanism responsible for prostatic regression following orchidectomy.

the long-term treatment of advanced prostate cancer with multiple hormonal agents. This assumption appears to be correct since virtually no side-effects associated with the use of diethylstilbestrol have been observed in the first few patients entered into the trial.

Even though all prostate cancer cells should be killed by such treatment, it is inevitable that some of them survive and grow back to give rise to life-threatening complications. Fortunately, it is becoming increasingly clear why a few cancer cells do in fact manage to survive powerful anti-hormone therapy. This is due to the fact that prostate cells may contain small sub-populations of specialized cells, some of which are protected against changes in the hormonal environment. In the past year, the Section has been successful in developing a model system which measures the number of such cells and for the first time affords an opportunity to study the impact of various types of therapy on the lethal component of the tumour.

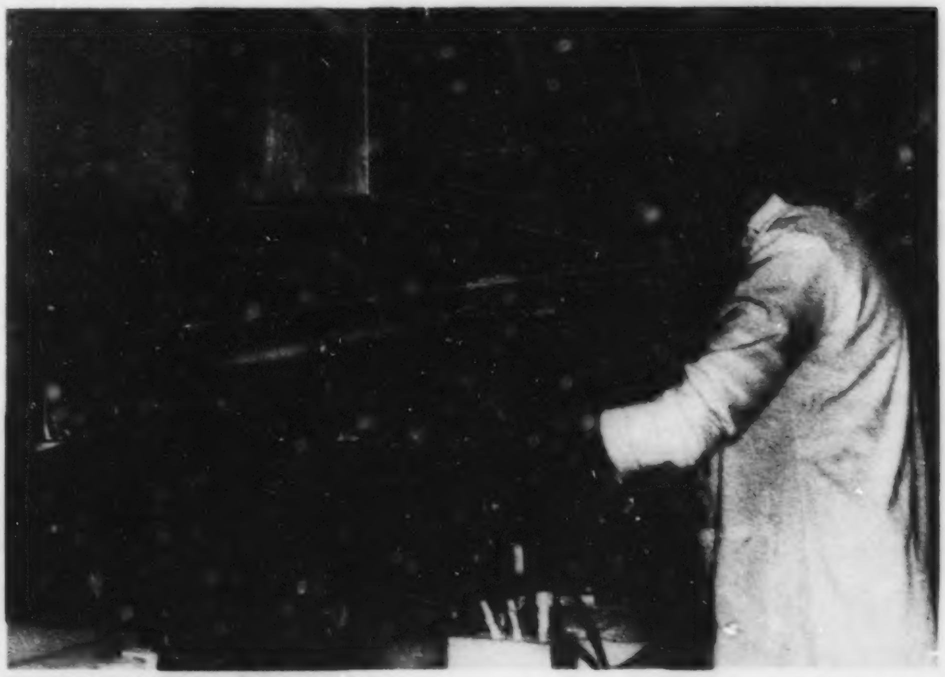
The Section benefits from collaborations with a number of investigators: Dr. D. Luck and Dr. M. Smith of the Department of Biochemistry, University of British Columbia, on the structure and function of prolactin; Dr. C. Sherlock, Department of Medical Microbiology, University of British Columbia, on the epidemiology of human papillomavirus infection of the cervix in British Columbian women with cervical neoplasia; Dr. J. Richards, Department of Biochemistry, University of British Columbia, on mitogenic stimulation of tumour cells by prolactin; Dr. M. Tenniswood, Department of Biochemistry, University of Ottawa, on programmed cell death; Dr. R. Buttyan, Department of Pediatrics, University of North Carolina, on the purification of the receptor protein for androgens; Dr. J. McNeal, Department of Urology, Stanford University, on metastatic potential of prostatic carcinoma; Dr. D. Russell, Department of Pharmacology & Therapeutics, University of South Florida, on the effects of immunosuppressive cyclopeptides; Dr. K. Hoshino, Department of Anatomy, University of Kyoto, on bioactivity of variant forms of prolactin; Dr. N. Emanuele, Edward Hines Jr. Hospital, Hines, Illinois, on hypothalamic forms of prolactin; Dr. V. Petrow, Department of Chemistry, Duke University, on the mechanism of action of 5a-reductase inhibitors; Dr. F. Batzold, Department of Endocrinology, Sterling-Winthrop Research Institute, on the inhibition of 5a-reductase activity in human prostate.

Operating grants in support of the basic and applied investigations have been received by Drs. Bruchovsky, Beer, Gout and Rennie from the Medical Research Council of Canada and the National Cancer Institute of Canada. The year was highlighted by an event of special significance. Dr. Noble received the 1987 Distinguished Service Award from the Canadian Society of Endocrinology and Metabolism in September 1987.

Dr. Bruchovsky presented lectures at the Symposium on "Prostatic Cancer: Current Practices and New Therapies", (Vancouver, British Columbia), the 3rd International Congress on Hormones and Cancer Satellite Symposium on "Prostate Cancer: Rationale of Endocrine Management" (Hamburg, Federal Republic of Germany), the Second Tokyo Symposium on Prostate Cancer (Tokyo, Japan), the Division of Biochemical Pharmacology, Shionogi and Co., Ltd. (Osaka, Japan); the Department of Urology, School of Medicine, Chiba University (Chiba-shi, Japan); and the Department of Pathology, University of Colorado Health Sciences Centre (Denver, Colorado). Dr. Rennie presented a lecture at the Third International Congress on Hormones and Cancer (Nice, France). He also served as a Chairman of Grants Panel D (Endocrinology) of the National Cancer Institute of Canada.

Drs. Gout and Beer attended the 69th Annual Meeting of the Endocrine Society U.S.A. (Indianapolis, Indiana) and also the Symposium on the "Biology of Growth Factors" (Toronto, Ontario) where they presented recent results of their studies on the progression of experimental hormone-dependent cancers. Dr. Gout presented a lecture in the Department of Pharmacology, College of Medicine, The University of Arizona, Tucson, Arizona. Visitors to the Section included: Dr. J. McNeal, Stanford University, Palo Alto, California; Dr. Ralph Buttyan, Columbia University, New York, New York; Dr. Imre Konyves, Leo Research, Helsingborg, Sweden; and Dr. Martin Tenniswood, University of Ottawa, Ottawa.

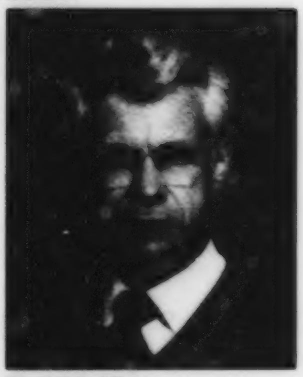
The Section has frequently drawn on support for its activities from the University of British Columbia, Departments of Medicine, Urology and Pathology, each of which has given generously of time and patient resources throughout the year.



Dona Lawson is 32p-labelling a probe to screen the MRNA of the androgen dependent tumor line, SSC. The aim of this study is to look at differential expression of such probes as c-myc, cfos and a probe for the A.R. in growing, recurrent and a recurrent tumor that has been transplanted back into intact male mice.

Advanced Therapeutics

STAFF:



Dr. H.K.B. Silver,
BSc, MD, PhD, FRCP(C), FACP
Head
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Dr. J.H. Goldie*

Dr. F.A. Salinas, BS, DVM
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Dr. S.R. Dedhar, BSc, MSc, PhD
Assistant Professor (Pathology)

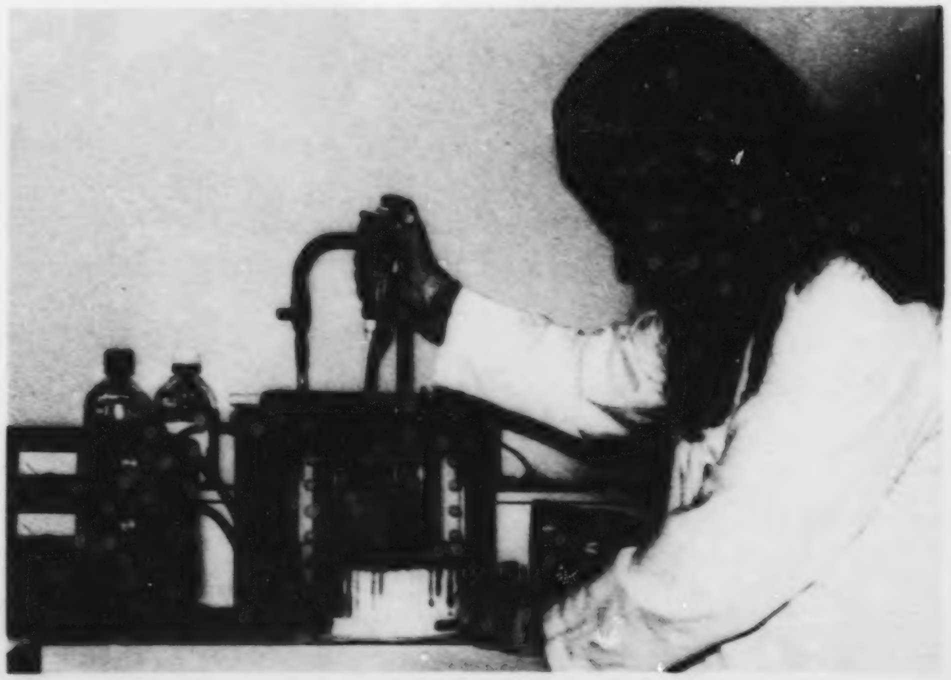
Dr. R.J. Klasa, MDCM, FRCPC

Initially conceived as a laboratory support arm of the Division of Medical Oncology, our basic research interests remain oriented toward clinical application. This integrated approach has resulted in productive basic research and served as an engine for many of the therapeutic advances in Medical Oncology. This is illustrated by our ongoing programs.

Laboratory support has been especially important in the use of biological response modifiers. The complex interaction of biological agents with the immunoregulatory network demanded close laboratory investigation to unravel the relationships among dose, route, schedule, immune interaction, and response. In our earlier interferon studies we were able to uncover relationships suggesting a strategy that led to improved survival in breast and ovarian carcinoma patients. Although our interleukin-2 studies are relatively young, we have early evidence that our spleen perfusion technique induces marked LAK cell activation at very modest doses and acceptable toxicity. If present trends continue this technique will be expanded as a relatively safe and simple method for immune adoptive transfer. These programs have brought new promising agents to our patients years before they would otherwise be available. We are planning to look at potentially important experimental agents such as GM-CSF, monoclonal antibodies, and possibly tumor necrosis factor.

Dr. Goldie is continuing his work on methotrexate resistance. Acute leukemia patients are now being screened to see if identification of resistant enzymes may be used to direct treatment. The same work has allowed a collaborative effort to identify novel folic acid antagonists. His theoretical model for chemotherapy resistance has been instrumental in the development of highly effective Agency treatment programs using intensive non-cross resistant chemotherapy. Additional studies are looking at the use of artificial intelligence and other advanced computing techniques in clinical oncology. The first phase, development of an interactive diagnostic tool for Hodgkin's Disease, has been completed. This experience is now being expanded to include more sophisticated analysis of clinical data.

Advanced Therapeutics has also been active in developing new techniques for the diagnosis and monitoring of cancer patients. For example our department, in collaboration with Dr. LaRiche, has become very adept at using the flow cytometer to analyze tumor samples for DNA content. In our most recent analysis we have found this to



Virginia Gray in Dr. Shoukat Dedhar's laboratory, is carrying out Polyacrylamide Gel Electrophoresis of cell-surface cell-adhesion receptors from human tumor cells treated with various growth modulators and Gly-Arg-Gly-Asp containing synthetic peptides.

Dr. K.A. Karim is seen here performing tests on blood samples from patients receiving Interleukin-2. These identify the extent to which the patient's immune system is activated to kill cancer cells.

be a powerful tool for the assignment of risk in malignant melanoma patients. Studies by others have suggested comparable predictive value for other tumor sites. Such analysis may be particularly helpful in designing effective adjuvant treatment programs. Our next step will be to expand this technology to look at nuclear c-myc oncogene expression.

With our group in the Radioimmunoassay Lab we have been able to introduce two new markers for clinical use, CA-125 and PSA. These provide significant improvements in the serologic detection and monitoring of cancer. This is a clinical service provided for physicians thoughout the province.

At a more basic level, Dr. Salinas is continuing his investigation of breast cancer antigen and related immune complexes.

We can also expect interesting developments from Dr. Dedhar's investigation of tumor cell interactions with extracellular matrix. Since cell surface receptors for fibronectin-related small polypeptides may determine the metastatic potential for a tumor, this may lead to prospective technique for evaluating metastatic potential. In related work Dr. Dedhar has been investigating growth factors, differentiating inducing factors and oncogene expression. This work could well be important for our biological response modifier program.

As these programs continue to develop we can look forward to further clinical application.

Epidemiology, Biometry & Occupational Oncology

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V.T.Y. Ng, MMath

The research activities of our Division, which consists of three sections and of the Breast Screening Centre, have been supported by grants amounting to $960,000 from the following sources: National Health Research Development Program, National Cancer Institute, Workers' Compensation Board of B.C., B.C. Health Care Research Foundation, National Institutes of Health and the B.C. Cancer Foundation.

In 1987, members of the Division published 25 papers.

Occupational Oncology Section

The occupational oncology program has been designed to identify, using a stepwise methodic approach, cancer risk factors and occupational carcinogens in the workplace. Two broad-based hypothesis-generating studies have been completed and published (one in press): "Occupation and Mortality in British Columbia" and "Geographic Distribution of Cancer in British Columbia".

Our major on-going study involves the collection, by means of a self-administered questionnaire, of life-time work history and smoking information on every male cancer patient aged 20 years and over ascertained by the British Columbia Cancer Registry. To date 14,000 questionnaires have been received and a preliminary report of the findings will be presented at the upcoming International Symposium on Occupational Cancer Epidemiology organized by our Division.

The establishment of a job-exposure matrix for the main industries of B.C. carried out with the Department of Chemical Engineering at UBC is progressing and should be completed within the next three years.

Final data on the cohort study of aluminum workers in Kitimat will be available this fall.

Epidemiology Section

The Section of Epidemiology has studies underway in a number of areas of research.

An ongoing program investigating the etiology of breast cancer as well as benign breast disease is yielding important scientific results. Male and female reproductive organs are the subject of another series of etiologic studies conducted in collaboration with the Fred Hutchinson Cancer Center in Seattle. A major paper on results from one of these studies recently appeared in the New England Journal of Medicine.

In collaboration with the Department of Social Work at CCABC, a program in psychosocial epidemiology was initiated last year and the first funded study is now underway.

An active melanoma research program is being carried out in conjunction with the Division of Dermatology. A study of benign nevi in school children is in the analysis phase. Results from this study may tell us whether it is possible to modify childhood lifestyle behaviour in order to lower risk of malignant melanoma later in life.

Our section is also involved in etiologic aspects of childhood and developmental cancers with studies on testicular cancer and cryptorchidism in childhood.

Vincent Ng demonstrates the B.C. Cancer Mapping program and explains how to extract information on cancer mortality rates for each school district in the province.

Further individual projects include a case-control study of colorectal cancer among North American Chinese in B.C., San Francisco and Los Angeles, and a collaborative Canadian study of thyroid cancer.

Biometry Section

The Biometry Section conducts research into the application of statistical and computer methods to problems of cancer and assists other cancer researchers in the Division and throughout the Agency in the design, analysis and presentation of their research projects.

In the past year the Section's members have been heavily involved with the occupational oncology program providing statistical and programming support for the Health in the Workplace project, directing the cohort study of the Alcan aluminum smelter in Kitimat, developing computerized record linkage techniques for occupational and administrative research, and providing computer programming support for the update of the occupational cancer mortality monograph.

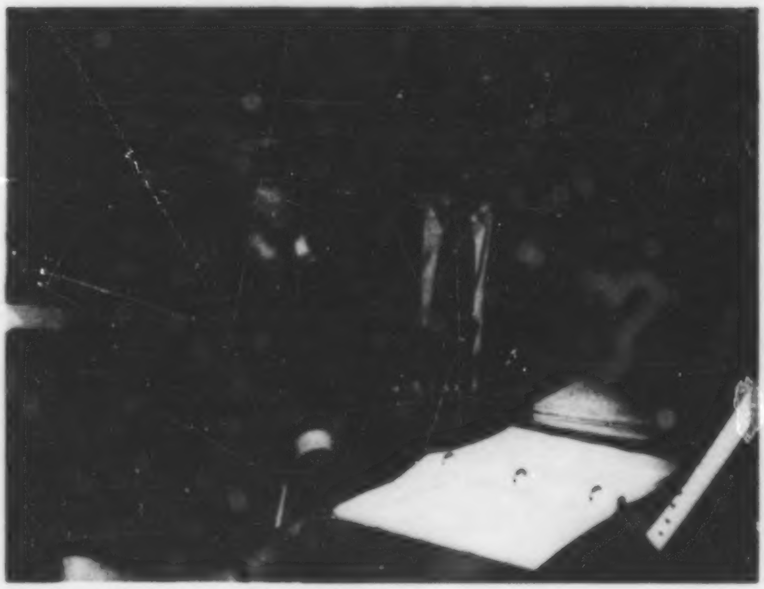
The Section has also contributed to the Epidemiology Section by providing statistical and programming support for studies including the identification of risk factors for testicular cancer and cryptorchidism, the examination of dietary and other etiologic factors in determining the risk of breast cancer, identification of prognostic factors in stage 1 malignant melanoma, the analysis of Native Indian mortality in B.C., the identification of risk factors for benign breast disease, and the determination of the prevalence of cancer in British Columbia.

Members of the Section also provide statistical and computer support to other researchers throughout the Agency. In addition to providing assistance in the design of a large number of clinical studies, the division has provided statistical support for several research projects. Recent studies include the identification of prognostic factors for Non-Hodgkin's lymphoma, the evaluation of a DNA index as a predictor for recurrence in melanoma, analysis of the effect of bone marrow transplant in the treatment of lymphoma, the evaluation of estrogen receptors as a prognostic indicator for breast cancer, the evaluation of pion therapy in cancer treatment, analysis of the effect of new treatment modalities for breast cancer, the evaluation of high-dose radiotherapy for the treatment of lung cancer, and the application of artificial intelligence in the diagnosis and treatment of Hodgkin's disease.

Breast Screening Centre

The Vancouver Breast Screening Centre is one of 15 centres participating in the NCIC research program aimed at determining whether screening women for breast cancer will reduce the death rate from the disease. Women aged 40 to 59 years were eligible for study and were randomized to receive annual mammography. All received instruction in breast self-examination and an initial breast physical examination by nurse examiners.

The Centre opened in March 1983 and closed in May 1988. Over 9,300 women entered the program in Vancouver and have been followed annually over the last five years. The response for rescreening and for questionnaire follow-up has remained very high over the duration of the program. The effect of screening on breast cancer mortality will not be known for several more years as these women will continue to be followed.



Anya Keefe from the UBC Chemical Engineering Department and Larry Svirchev examine data on the Job Exposure Matrix, which is aimed at linking chemical exposures to job titles for the main industries of B.C.

Diana Raynor discusses with a patient details of his work history.

Joint Animal Facility

The Joint Animal Facility is supported financially by the B.C. Cancer Foundation, the Cancer Control Agency of B.C. and the University of British Columbia.

This spring there was an on-site evaluation by the Canadian Council on Animal Care. The high quality of animal care for the past six years will be continued into our seventh year of operation. Special thanks to Fred V. Jensen and Sandy Mills.

Currently the members of the Joint Animal Facility Management Committee which oversees the operation of the animal facility are Dr. P.W. Gout, Dr. D.J. Chaplin, Dr. F. Salinas, Dr. A. Eisen and Dr. J. Love.

Dr. P.W. Gout,
Chairman

Mr. F.V. Jensen,
Senior Technician

Master Publications List 1987-88

ADVANCED THERAPEUTICS

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British Columbia Cancer Foundation

B.C. CANCER FOUNDATION
CANCER RESEARCH CENTRE
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British Columbia Cancer Foundation

The British Columbia Cancer Foundation is a society incorporated under the "Societies Act" of British Columbia and is registered as a charitable organization under the provisions of the "Income Tax Act" of Canada. The Foundation, which owns and operates the British Columbia Cancer Research Centre, as at August, 1984, also became the Foundation for the Cancer Control Agency of British Columbia, which operates cancer clinics throughout British Columbia. As such, the British Columbia Cancer Foundation is responsible for raising the supplementary funding needed by the Cancer Control Agency for items such as capital equipment not covered by provincial government grants.

The Foundation is totally dependent upon the generosity of the citizens of British Columbia to meet its cancer research and treatment commitments. You can support the work of the British Columbia Cancer Foundation by making a private or 'in memoriam' donation or by making the Foundation a beneficiary in your will. Donations are deductible for income tax purposes and may be made directly to:

British Columbia Cancer Foundation
601 West 10th Avenue
Vancouver, B.C.
V5Z 1L3
Tel: 877-6010

The Foundation accepts both MasterCard and VISA.

All donations to the B.C. Cancer Foundation remain in B.C. to be used in the development of research, diagnosis and treatment which will be of direct benefit to cancer patients in the province.

A receipt will be issued, including the prescribed information, for purposes of the "Income Tax Act".

The British Columbia Cancer Foundation is most grateful to those whose generosity helps in the ongoing fight against cancer!

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President's Report

Victor F. MacLean – President

This has been a challenging year for the British Columbia Cancer Foundation. Cancer is on the increase in British Columbia as it is everywhere, consequently there are increasing costs and expanding demands on our resources. The cost of diagnosis, treatment and cancer research, the cost of replacing old equipment with new, all continued to show increases in 1987/88, while the B.C. Cancer Foundation faced a serious deficit. Strenuous efforts were made by the Board of Directors, the Executive Committee and our standing committees to address this problem. But in light of the total situation, it called for stringent financial controls, cutbacks in some operations and the curtailment of new initiatives. As a consequence it is a pleasure to report that through the cooperation and the dedicated efforts of all concerned – the Executive and the committees of the Foundation, the Board of Directors of the Cancer Control Agency of B.C., Unit and Division Heads of the Research Centre, and the Administration and Financial staff of the Cancer Control Agency of B.C. – progress has been made in the financial affairs of the Foundation and we are able to forecast a balanced budget for the year ahead.

In order to reduce costs and to streamline the operations of the Foundation, it was necessary to make major staff reductions and merge financial and administration operations with the Cancer Control Agency of B.C. In November, David Catton, who had been appointed Director of Development in 1985, accepted the responsibility as Executive Director of the Foundation. He continues to serve in the dual capacity of fundraiser for the Foundation.

In July, Dr. David Klaassen commenced his appointment as Director of the Cancer Control Agency of B.C. In addition to this major responsibility, he has been of considerable assistance in the affairs of the Foundation.

The newly structured Research Management Committee replaced the Foundation's old Research Committee. Under Dr. Klaassen's chairmanship, the Research Management Committee has assumed more direct advisory management responsibility for the Research Centre. As an economic measure, and because it was facing heavy competition from laboratories in eastern Canada which would have called for a heavy infusion of capital in order for it to remain in operation, the Carcinogen Testing Laboratory, an arm of the Environmental Carcinogenesis Unit, was closed down. The prospect of satisfactory revenue over the previous three years was never achieved.

One of our long term objectives for the Research Centre has always been to develop a closer working relationship with the Cancer Control Agency of B.C. Under David Klaassen's leadership, this appears to be happening. In no way is there any sense of reducing or diminishing those aspects of pure research which are so essential to the future of cancer research but there are a number of research protocols underway, either in the laboratory or in the clinical trial phase which, it is hoped, will be of direct benefit to patients. From the point of view of the Foundation, the patients of the Clinic, the provincial government which funds diagnosis and treatment and therefore has to be keenly interested in advances in treatment, and our donors and supporters, such an enhanced working relationship is of the utmost importance.

Our scientists continue to receive international recognition for their work. They are widely published at home and abroad and lecture extensively in Asia, and Pacific Rim countries as well as Europe and the U.S.A. It is gratifying to report that a number of research initiatives developed at the B.C. Cancer Research Centre are now under joint investigation at other centres and hospitals in the United States and overseas. It is this constant sharing of ideas and initiatives which is keeping Vancouver in the forefront of cancer research worldwide and we can take genuine pride in the work and the achievements of our scientists.

While the B.C. Cancer Foundation is responsible for the global budget required to operate and maintain the laboratories and equipment at the Research Centre, our scientists continue to attract sizeable project grants from the major granting bodies for cancer and medical research. These are the National Cancer Institutes of both Canada and the United States, the Medical Research Council of Canada, the B.C. Health Care Research Foundation, the United States National Institutes of Health, the Vancouver Foundation, the Woodward Foundation, the Jambor Knowledge Fund together with the generosity of a number of individual donors. We continue to work closely with our other major partners in the field such as the Canadian Cancer Society, the University of British Columbia and Simon Fraser University.

On the fundraising front, as in prior years, donations, bequests and "in memoriam" gifts provided the major source of funding for the Foundation. We are deeply indebted to our many individual donors, large and small for their continuing generous support of the work of the B.C. Cancer Foundation.

In the year under consideration, the B.C. Cancer Foundation in conjunction with the Cancer Control Agency of B.C. attracted the single largest bequest in its history from a member of the medical profession. Dr. Esther Brown, herself a physician at the Cancer Control Agency of B.C. died of breast cancer and left an estate of approximately $2.5 million to be used largely by her fellow radiation oncologists to further their own work at the Clinic.

In direct fundraising activities, we entered the second year of the Allied Corporate Crusade Against Cancer partnership with the Canadian Cancer Society, B.C. and Yukon Division, and while our goal has not yet been reached in this campaign, we anticipate that final returns will be somewhat ahead of last year. Together with the Canadian Cancer Society, B.C. and Yukon Division, the Foundation has pioneered in Canada with this joint campaign to reach the corporate community, and we are confident that it will continue to grow and develop in the years ahead. Major contributions from the corporate sector are essential if we are to continue the battle against cancer. In this campaign, we are indebted to some two hundred volunteer canvassers under the capable leadership of Dale Parker, Chairman and C.E.O. of B.C. Bancorp, and with the Honourable Nathan Nemetz, the retiring Chief Justice of British Columbia, as Honorary Chairman. Our grateful appreciation to those who contributed of their time and effort.

A highly successful theatre evening featuring the international production of CATS generated $50,000 and we will be participating in similar special events in the future. This year we are particularly appreciative of the support and funding assistance from the Canadian Cancer Society, B.C. and Yukon Division.

On closing, it is important to emphasize and thank the Foundation Board Members and Executive Committee together with the several standing Committees for their attendance, assistance, and support throughout this past year, and to all those employees and administrative personnel who have assisted in the turnaround in the Foundation affairs. A special note of appreciation to the Cancer Control Agency of B.C. for the new positive working relationship which has been of immeasurable assistance in the past year.

Victor F. MacLean
President
B.C. Cancer Foundation

Bursary, Scholarship & Awards Committee

The Bursary, Scholarship & Awards Committee met in March to review a total of 20 studentship applications for the May-August term. A single studentship application for the Fall term was reviewed in June. As in the past, awards were granted on the basis of each student's qualifications as well as the quality and relevance of the proposed project in the field of oncology.

I am pleased to report that a total of 12 studentship awards were granted, including the J.M. Warren and A. Maxwell Evans Awards.

The studentship recipients for 1988 are: Erika Cheng, Gerald James, Videsh Kapoor, Dicken Ko, Leslie-Jean MacMillan, Chrystal McNabb, Simon Min, Sheldon Morris, Nanette Mortil, Paul Sobkin, and Stephen Tiu. An alternative opportunity arose for one student, who subsequently declined the B.C. Cancer Studentship.

Every year, the A. Maxwell Evans and J.M. Warren Awards are granted to two outstanding students. This year, Mr. Ben Yokoyama was awarded the A. Maxwell Evans Award, on the advice of the Faculty of Medicine, University of British Columbia. Mr. Yokoyama is working with Dr. H. Pritchard of the Faculty of Medicine on a research project titled "Magnetic Resonance Spectroscopy of Plasma: Evaluation as a screen for cancer and identification of the molecular basis of the abnormal signal in malignancy."

For the second year, the J.M. Warren award was granted to Miss Nancy Goodchild, the highest ranking studentship applicant. This year, Miss Goodchild is working with Dr. Dixie Mager of the Terry Fox Lab on a research project titled "Genomic Stability of Human Endogenous Retrovirus-Like Sequences".

The students will be working under the supervision of senior scientists who are affiliated with the B.C. Cancer Research Centre, the University of British Columbia and the University of Victoria.

Funding for these awards is provided by the B.C. Cancer Foundation and the Canadian Cancer Society.

During 1987-88, the British Columbia Cancer Foundation approved 14 travel grants to graduate students. These grants were established to help defray travel costs when graduate students are invited to attend conferences to present their work in the field of cancer research.

Both the studentship program and the travel grants are important to the British Columbia Cancer Research Centre. They enable us to recognize academic excellence and to encourage promising young people to pursue a career in oncology.

Finally, the Committee has conducted an extensive review of both the application form and evaluation procedures. A number of changes were recommended which will help to streamline the process and will also bring our 'calendar' in line with that of the universities.

I would like to thank the members of the Committee for their guidance and assistance in making this educational program a success: Dr. N. Auersperg, Dr. G. Ballantyne, Dr. R.E. Beck, Dr. D. Mager, Dr. B. Palcic, Mr. P. Tulk, Dr. P. Rennie, Dr. H. Stich, Mr. V.F. MacLean, Mr. D. Morrison and Mr. D. Catton.

Anna Linsley
Chairman

Research Management Committee

The Committee advises the B.C. Cancer Foundation on scientific matters and meets monthly to discuss research management issues in the B.C. Cancer Research Centre. It reports to the Executive Committee of the Foundation.

Issues considered this past year included the creation of the Cancer Imaging Section; a level "D" containment laboratory; revenue generating activities; a patent policy for the Foundation and the Cancer Control Agency; the need for a biohazard safety officer; and space allocation within the Centre.

A review of the scientific staff salary scale was carried out by the consulting firm of Towers Perrin and, after modification, was recommended to the Foundation.

The scientific staff participated in the strategic planning process of the Agency and, with the Committee, provided help and advice on the reorganization of the Research Centre and on the budgetary-financial issues of the Centre and its Foundation.

I appreciate the contribution of the members of this Committee: Dr. P. Band, Dr. N. Bruchovsky, Dr. A. Eaves, Dr. G. Goodman, Dr. R. Kornelsen, Mr. V. MacLean, Dr. H. Silver, Dr. L. Skarsgard, and Dr. H. Stich.

On behalf of the Committee, I thank Mr. D. Catton, Mr. R. Smith, Ms. R. Bruce and Mr. D. Richardson for administrative support. Thanks are also due to Ms. B. Prieur for secretarial support and help.

D.J. Klaassen, MD, FRCPC
Chairman,
Research Management Committee

Women's Auxiliary

The Women's Auxiliary to the B.C. Cancer Foundation and the Canadian Cancer Society (B.C. and Yukon Division) and the A. Maxwell Evans Clinic is now in its 42nd year of service.

Our members continue to contribute service in a variety of ways. We have Escorts whose main function is to accompany new patients from the Admitting Department to the Ambulatory Care Unit, laboratories or treatment areas. The Aides in the treatment and outpatient clinics assist patients and staff. Ladies of the Patient Aide group serve coffee and juice to patients waiting for treatment in the Radiotherapy Department. Current magazines are distributed throughout the Clinic and the "candy-wagon" volunteers make rounds through the Clinic and the hospital units twice weekly. Volunteers visit out-of-town patients who are confined to the hospital unit for an extended period. Our talented sewing group continues to make head scarves, tracheotomy bibs and pouches for chemotherapy pumps. These are provided to the patients at no charge. Auxiliary members continue to provide patient support at TRIUMF.

Membership was down this year so an effort was made to recruit new volunteers. Thirty notices were sent to various churches, newspapers, television and radio stations. We received a good response and have been able to interview and place nine new volunteers. At our annual meeting last April, Mrs. Rogers, our Honorary Patroness, presented two of our volunteers with long-service pins; one was for twenty years and the other for fifteen years of service.

This year we have a change in our liaison with the administration. In the past we have enjoyed working with Mr. David Richardson and his staff. We would like to take this opportunity to thank Mr. Richardson and the members of his staff for their assistance and support. Our liaison now is with Mrs. Bonnie Jamieson, Assistant Deputy Director of Nursing and Related Patient Care Services. We look forward to working with Mrs. Jamieson in the coming years.

Christmas is a busy but special time of year for us. We decorate the Clinic and distribute poinsettias. The number of baskets we distributed to hospital and outpatients increased this year because of the expansion of the Lodge. These baskets are filled with home baking, fresh fruit, candy and special teas and are accompanied with a knitted bedjacket or slippers. In addition, food vouchers were given to some patients on the advice of the Social Work Department.

Since we are a non-fund raising organization, we are grateful for the financial support of the Foundation and the Society. As a representative of the Auxiliary, it has been my privilege to serve on the Board of Directors of the Cancer Society and the Foundation and to attend the Board of Trustees meetings of the Cancer Control Agency. This has given me a comprehensive understanding of the functions of each organization.

The members of the Auxiliary look forward to continuing and expanding service to the comfort of cancer patients as well as to maintaining our good working relationship with the Society, the Foundation and the Clinic.

L. Thompson
President, Women's Auxiliary

Finance Committee

For the third consecutive year our revenues failed to meet the ever-increasing demands on the Foundation to provide funds to support important ongoing and exciting new research projects, both at the B.C. Cancer Research Centre and in support of the Cancer Control Agency of B.C.'s clinical-oriented research programs.

The Foundation, over this period of time, budgeted expenditures based on oral agreements that substantial funding would be forthcoming. These arrangements did not materialize.

As indicated in the accompanying financial statements, our plan for fiscal 1988/89 provides for a modest surplus of $144,000 compared to our 1987/88 deficit of $565,000. This will be accomplished partly as a result of the two-year-old fundraising initiatives, partly as a result of being able to have some research program costs undertaken by allied agencies and, unfortunately, by reduction of our support of some programs.

The Foundation's mandate is to aggressively increase the level of funding from our various publics in order to meet the needs of those we support in the extraordinary new and continuing research and development programs in preventing, controlling and curing cancer.

On behalf of members of the Finance Committee, Messrs. V.F. MacLean and F.B. Moore, I thank for their support, Ms. Sharon Kennedy, Messrs. D.S. Catton, D. Morrison and our auditors, Price Waterhouse.

Ian M. Adam
Chairman
Finance Committee

Student Research Awards

Genomic Stability of Human Endogenous Retrovirus-Like Sequences

The study of retroviruses has led to an increased understanding of many fundamental problems in biology including gene regulation and the genetic basis of cancer. Some retroviruses carry genes (oncogenes) that cause cancer in animals and retroviruses are causative agents for adult T-cell leukemia and AIDS in humans. Upon infecting a cell, the viral RNA genome is copied into DNA which integrates into a cellular chromosome. If this event occurs in a germ line cell, the integrated retrovirus becomes endogenous to the host organism and will be inherited from parent to offspring like other normal genes. Endogenous retrovirus-like sequences are widespread in the animal kingdom having been found in species ranging from reptiles to mammals. Some are the remnants of ancient germ line infections while others may be cellular entities that are evolving toward true retroviruses. In the mouse, these types of sequences can transpose or insert into new locations in the genome thereby altering the functions of important cellular genes. Indeed, there is evidence that mouse endogenous retroviruses may contribute to tumor development by activating cellular proto-oncogenes through insertional mutagenesis.

Recent results indicate that the normal human genome contains a complex variety of endogenous retrovirus-like sequences. One particular family of such sequences, termed RTVL-H, has a very high copy number of approximately 1000, suggesting that these sequences had (and may still have) the capacity to rearrange in the genome. The goal of this summer project is to examine the stability of the RTVL-H family of sequences in human cells. Specifically, the project will involve identifying DNA polymorphisms or differences that may be associated with particular RTVL-H sequences. To achieve this aim, six available non-repetitive DNA probes derived from the flanking regions of six different RTVL-H elements will be used. Also available in the Terry Fox Laboratory are DNA samples from at least 100 unrelated individuals. In addition, DNA samples from both the normal fibroblasts and the leukemic cells of approximately 30 leukemic patients are available. Restriction enzyme digests of these DNAs will be screened with the RTVL-H flanking probes using Southern transfer and molecular hybridization techniques. The hybridization patterns will be examined for differences between individuals as well as differences between the normal and leukemic cells from the same individual. Any differences between DNA samples will be examined with further hybridization studies to determine if it represents a rearrangement of the RTVL-H sequence adjacent to the probe.

Although this protocol will test for genomic polymorphisms of only a few of the many RTVL-H sequences, the frequency of differences detected with the six randomly chosen probes will give us an overall indication of how variable these sequences are between individuals. Furthermore, by screening normal and leukemic cells from a set of patients, we can begin to determine if RTVL-H sequences undergo rearrangements in malignant cells which are generally more genetically unstable than their normal counterparts. Taken together, the results of this project will be useful in assessing the possible role that endogenous retrovirus-like sequences may play in the genetic changes involved in the induction or progression of malignant disease.

Nancy Goodchild
J.M. Warren Studentship Award

MAGNETIC RESONANCE SPECTROSCOPY OF PLASMA:

Evaluation as a screen for cancer and identification of the molecular basis of the abnormal signal in malignancy.

A. BACKGROUND

There is a growing body of evidence which suggests that the determination of the ^{1}H-NMR linewidth of lipoprotein resonances of blood plasma samples may provide a screening blood test for cancer. This has resulted from the observation that the methylene and methyl linewidth signal of plasma lipid is significantly reduced in patients with malignant tumors when compared to controls. The biophysical and biological mechanism involved is not known at present but probably involves increased levels of plasma triglyceride and/or malignancy associated lipoproteins.

B. AIMS

1. To establish the basic MRS detection method by analysis of ^{1}H-NMR lineshape changes in serum samples from patients with malignancy and from normal individuals.
2. To establish the interassay and intraassay reliability for this technique.
3. To investigate the sensitivity of the assay to the detection of malignancies at very early stages. Specifically, we will analyze the signal from plasma of newly diagnosed patients with carcinoma of the cervix, prostate and breast.

4. To compare with presently available serologic technique by coanalysis of the level of squamous cell carcinoma antigen, prostate specific antigen and CA 15.3 antigen.
5. To investigate the relationship between plasma lipid levels and the detection of malignancy by MRS of plasma lipoprotein.
6. To determine the molecular basis of the abnormal signal: evaluation of the relative contribution of increased VLDL and malignancy associated lipoproteins.

C. SIGNIFICANCE

This study will provide a detailed analysis of the application of MRS to the detection of malignancy. Correction for overlaying factors such as diet and endogenous dyslipoproteinemias should provide novel information on the factors giving rise to reduced ^{1}H-NMR plasma linewidth signal. This may lead to a more sensitive specific test for cancer as well as providing further insights into neoplastic cell metabolism and the metabolism of the plasma lipoproteins.

Ben Yokoyama
A. Maxwell Evans Studentship Award

Financial Statements

May 20, 1988

Auditors' Report

To the President and Board of Directors,
British Columbia Cancer Foundation:

We have examined the balance sheets of the general and designated funds and the British Columbia Cancer Research Centre fund of the British Columbia Cancer Foundation as at March 31, 1988 and the statement of changes in the general and designated fund balances for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests and other procedures as we considered necessary in the circumstances, except as explained in the following paragraph.

The Foundation derives part of its revenue from the general public in the form of donations which are not susceptible to complete audit examination. Accordingly our work in respect of this revenue was limited to accounting for the amounts recorded in the books of the Foundation.

In our opinion, except for the effect of adjustments, if any, which might have been necessary had the scope of our examination not been limited as referred to in the preceding paragraph, these financial statements present fairly the financial position of the Foundation as at March 31, 1988 and the results of its operations for the year then ended in accordance with accounting principles described in Note 2 applied after giving retroactive effect to the accounting change described in Note 3, on a basis consistent with that of the preceding year.

The 1988-89 planned results included in the statement of changes in general and designated fund balances have been prepared by management. We have not reviewed or audited these figures and accordingly do not express an opinion on them.

Price Waterhouse
Chartered Accountants

Balance Sheet
General And Designated Funds

	March 31 1988	 1987
Assets		
Current assets:		
Cash	$ 192,186	$ 8,442
Investments, at cost which approximates market	1,784,854	1,955,855
Amounts receivable (Note 4)	374,728	592,414
Inventory	65,615	102,493
	2,417,383	2,659,204
British Columbia Cancer Foundation Endowment Fund (Note 5)	729,000	727,000
	$3,146,383	$3,386,204
Liabilities and Fund Balances		
Current liabilities:		
Due to Cancer Control Agency of British Columbia	$ 490,514	$ 122,782
Accounts payable and accrued liabilities	95,945	52,305
Deferred revenue	–	52,457
	586,459	227,544
Fund balances:		
General	631,290	1,195,907
Designated	1,928,634	1,962,753
	2,559,924	3,158,660
	$3,146,383	$3,386,204

APPROVED BY THE BOARD:

Director

Director

Balance Sheet
British Columbia Cancer Research Centre Fund

	March 31 1988	 1987
Assets		
Land, buildings and improvements, at cost (Note 6)	$4,155,688	$3,990,716
Fund Balance		
Fund balance	$4,155,688	$3,990,716

Statement of Changes in General and Designated Fund Balances

	Plan 1988/89 General Fund	Year ended March 31, 1988 General Fund	Year ended March 31, 1988 Designated Fund	Year ended March 31, 1988 Total	Year ended March 31, 1987 General Fund	Year ended March 31, 1987 Designated Fund	Year ended March 31, 1987 Total
	(unaudited)						
Fund balances at beginning of year	$ 631,290	$1,195,907	$1,962,753	$3,158,660	$1,974,786	$1,263,381	$3,238,167
Additions:							
Revenue –							
Bequests	820,000	754,798	105,583	860,381	512,787	41,771	554,558
Donations	300,000	284,154	198,864	483,018	254,555	947,602	1,202,157
Investment income	246,450	260,100	116,356	376,456	231,075	112,856	343,931
Fees from services	357,000	156,727	–	156,727	622,317	–	622,317
Canadian Cancer Society – Conquer Cancer Campaign	130,000	100,000	–	100,000	75,359	–	75,359
Studentships	20,000	27,412	–	27,412	25,905	–	25,905
Fund Raising Projects – net of direct expenses	116,637	77,854	–	77,854	–	–	–
Other	63,411	140,512	(40,187)	100,325	41,728	156,916	198,644
	2,053,498	1,801,557	380,616	2,182,173	1,763,726	1,259,145	3,022,871
Deductions:							
Expenses –							
Research –							
Core Support Units –							
Cancer Imaging Unit	106,402	176,220	–	176,220	3,936	–	3,936
Environmental Carcinogenesis Unit	155,744	177,274	–	177,274	195,599	–	195,599
Medical Biophysics Unit	368,207	457,949	–	457,949	502,404	–	502,404
B.C. Cancer Research Centre – net of recoveries	586,521	600,699	–	600,699	801,535	53,326	854,861
Laboratory and other services	377,671	450,568	–	450,568	569,499	–	569,499
Cancer Control Agency of B.C. support	9,800	199,147	314,049	513,196	117,382	352,824	470,206
Designated projects	–	–	197,478	197,478	–	168,213	168,213
General administration (Note 7)	209,041	262,624	–	262,624	297,614	–	297,614
Other	96,000	41,693	(96,792)	(55,099)	54,636	(14,590)	40,046
	1,909,386	2,366,174	414,735	2,780,909	2,542,605	559,773	3,102,378
Change in fund balances	144,112	(564,617)	(34,119)	(598,736)	(778,879)	699,372	(79,507)
Fund balances at end of year	$ 775,402	$ 631,290	$1,928,634	$2,559,924	$1,195,907	$1,962,753	$3,158,660

Notes To Financial Statements

March 31, 1988

1. Nature of operations:

The Foundation funds and operates the British Columbia Cancer Research Centre facility.

The Foundation allocates its revenues as follows –

Operating funds –

(a) General Fund –

This fund receives all revenues which are not specified or designated at source as to their use. The Executive of the Foundation from time-to-time commits certain of these revenues to specific projects of the British Columbia Cancer Research Centre Fund and the Cancer Control Agency of British Columbia.

(b) Designated Fund –

This fund includes bequests, donations and investment income which are designated for a specific use by the donor.

British Columbia Cancer Research Centre Fund –

This fund represents the cost of the Foundation's investment in fixed assets of the Research Centre.

2. Accounting policies:

The Foundation's accounting policies follow generally accepted accounting principles except that –

Income from bequests and donations is recorded when received.

Land, buildings, and improvements held for research purposes are capitalized in the British Columbia Cancer Research Centre Fund at cost and no depreciation is charged.

3. Accounting change and comparative amounts:

The 1988 operating results have been condensed to show activity by principal functions. Previously, operations were reported by sources of funds and related expenditures. This change has resulted in a restatement of 1987 comparative figures. As part of the restatement, the Special Fund was eliminated by reclassifying external sources of funds restricted to specific projects to the Designated Fund and reclassifying internally designated funds to the General Fund.

The Foundation also administers investigative grants awarded by various private and public institutions to scientists for specific research projects undertaken at the Research Centre. In 1987 the receipts and expenditures with respect to these projects were included in the statement of changes in general, special and designated fund balances. Effective in 1988, these grants are now accounted for on a net basis to the extent that the Foundation has made advances on behalf of the funding institutions. This change reflects the custodial nature of the Foundation's role. These amounts are included in amounts receivable in the general and designated funds balance sheet (Note 4).

Revenues and expenses arising from the service activities of the Foundation have been combined and shown as separate revenue and expense items. Previously, each service activity was shown as an individual item on the statement of changes in general and designated funds.

The Capital Fund has been renamed the British Columbia Cancer Research Centre Fund and is shown as a separate balance sheet.

4. Amounts receivable:

Amounts receivable include advances on behalf of awards to investigators for research projects –

	1988	1987
Advances at beginning of year	**$ 191,398**	$ 83,662
Expenditures	**1,092,129**	1,157,985
	1,283,527	1,241,647
Receipts	**1,075,428**	1,050,249
Advances at end of year	**$ 208,099**	$ 191,398

5. British Columbia Cancer Foundation Endowment Fund (the Fund):

The Fund is administered by the Vancouver Foundation with the British Columbia Cancer Foundation receiving the income generated from the Fund after deduction of administrative costs. Under the terms of the agreement, the British Columbia Cancer Foundation will be entitled to withdraw all of its contributions to the Fund after 1990 with the exception of $10,000 initially contributed and expensed by the British Columbia Cancer Foundation in 1981. The capital in the Fund amounted to $1,154,000 at March 31, 1988 (1987 – $1,152,000) of which $739,000 was contributed by the British Columbia Cancer Foundation and $415,000 by the Vancouver Foundation.

6. Fixed assets:

During the year $164,972 (1987 – $88,182) of fixed assets were capitalized, of which $90,735 was reimbursed by the Cancer Control Agency of British Columbia. The portion paid for by the Foundation ($74,237) has been expensed in the General Fund.

7. General administration expense:

	1988	1987
Salaries	**$105,558**	$ 74,679
Office and general	**43,178**	44,899
Legal and audit fees	**40,387**	88,355
Funding and development	**73,501**	89,681
	$262,624	$297,614

8. Statement of changes in financial position:

A statement of changes in financial position has not been presented as it is not considered meaningful in the circumstances.

Donations and Bequests

for the period April 1, 1987 to March 31, 1988

The following donations and bequests are acknowledged with thanks:

Mackenzie Compact Car Centre	100
Air Canada RSUNS.	165
United Way of Central Fraser Valley	1,272
Parkland Reunion Graduates	234
B.C. Hydro Employees' Committee	119
Cancer Control Unit HEU Local 180	100
Geotechnical Materials Branch	210
Consulat General de France	100
United Way of the Lower Mainland	23,853
Macmillan Bloedel Limited	100
R. Cook Ventures Inc.	100
Fraternal Order of Eagles – B.C. Provincial Auxiliary	34,553
Davis & Company	3,500
The Dolly Toy Company	100
B.C. Prov. Aerie F.O. Eagles	1,125
Royal Canadian Legion Shalom #178	1,000
Owen Bird	200
Royal Canadian Legion Ladies Aux – Gold River	100
The Pegepolkin Family	100
Staff-Information Services Dept. – I.C.B.C.	191
Latvian Relief Society of Canada	165
Dynequip Engineering Ltd., Vice Pres.	150
Charles Hotel Restaurant	100
Radd Holdings Ltd.	1,000
Scott Paper Limited	500
Fitness Plus Consulting & Promotion	100
Louis Bros Roping	100
Children's Hospital	200
Anaesthesia Research Fund	100
Children's Hospital Operating Room	125
Royal Canadian Legion – L.A. Branch No. 2	200
S.C. Morris	500
Victoria High Grad '77	100
B.C. Prov. Aerie F.O. Eagles	5,000
B.C. Prov. Aerie F.O. Eagles	2,150
TY-Crop Welding & Mfg. Ltd.	100
St. Peter's Anglican Church	100
Pacific Press, Classified Advertising	105
Gough Electric	500
Vanlin Holdings Ltd.	2,000
British Columbia Masonic Foundation	400
Mary T. Spankie	200
Air Canada Passenger Service	168
Lawson, Lundell, Lawson & McIntosh	200
Marty's Limited	100
Dauphinee, Joe & Company	200
L.J. Lefohn Family Foundation	125
Sunshine Hills Elementary School	149
Vancouver Free Press Publishing Corp.	500
Order of the Eastern Star	150
Pacific Coast Title Search Ltd.	100
Land Title Office	195
McMillan Bloedel Staff	100
Andrew Mahon Foundation	800
Stevens, Barbara	100
CHQM Broadcasting Ltd.	250
Donald Flooring Contract Sales Ltd.	150
Northwest Musical Services Ltd.	100
Twelfth Avenue School Staff	110
Greater Victoria Hospital Society	1,050
Cdn. Inst. of Travel Counsellors (B.C.)	300
Kamloops Central Lions Club	3,295
Canadian Airlines International	4,304
Heritage Office Furnishings Ltd.	100
Commerce Undergraduate Society, Social Coord	200
Teamsters Local Union 464	100
Collingwood Elder Citizen's Centre	165
H.E.U. Local 180	100
Greater Victoria Hospital Society	100
B.C. Morgan Horse Club	4,000
D. McDonald Ltd.	250
Vaughan Properties Inc.	100
E.B. Ceramic Tiles	200
Fraternal Order of Eagles	555
University of B.C.	100
Dowa Mining Co. Ltd.	100
Adam, Mr. Ian M.	100
Aitken, Mr. William C.	500
Albinson, Mr. Joseph C.	100
Alexander, Ms. Joy	500
Archer, Ms. Betty	150
Backler, Mr. Brian B.	200
Ballantine, Ms. Jeannie	100
Barr. Mr. & Mrs. L.M.	300
Battista, Mr. Giuseppe	100
Bell, Mr. Gordon	150
Bentley, Ms. A.R.	150
Biasutti, Reno J.	250
Bigland, Mrs. Eva	100
Birks, Mrs. Joan D.	100
Black, Ms. Katherine I.	100
Blair, Mr. Robert W.	100
Bourne, Dr. & Mrs. Neil	100
Bourne, Ms. Jean	200
Bowie, Dr. Iain	100
Brakenridge, Ms. Jean	100
Brazier, C.W.	600
Brissenden, Mr. P.R.	200
Brockhouse, Mr. G.	100
Brody, Mr. H.	200
Brown, Mr. W. Thomas	100
Brown, Mr. Joseph F.	200
Browne, Mr. G. Ralph	500
Burley, Mrs. A.	100
Butler, Ms. Jane	100
Callow, Mr. S.	100
Carlow, Mr. & Mrs. Mel	100
Chance, Mr. Brian K.DE.P.	100
Chatzigiannis, Mrs. Maria	110
Christian, Mr. John	200
Clyne, Mr. John	200
Coghill Thorne, Ms. Joy	100
Collins, Mrs. Bessie	100
Connop, Mrs. V.M.	1,000
Cook, Mr. Philip T.	100
Coughtry, Ms. Lillian M.	100
Coy, Dr. Peter	100
Crowhurst, Mr. J.J.	1,050
Cumming, Miss Jean	400
Dafoe, Mrs. J.E.	100
Dafoe, Mr. Richard	100
Davidson, Lori	100
Deering, Mr. Edward	100
Demmery, Dorothy & Annie	200
Diggle, Mrs. Rose	100
Doran, Mrs. Clyde	200
Dumoulin, Mr. Michael L.	1,000
Dunlop, Mrs. A.I.	100
Easton, Mr. A.W.	1,000
Edwards, Mrs. Frances M.	100
Erskine, Mrs. Audrey M.	3,000
Falconer, Mr. D.W.	100
Farley, D.J.	100
Fehr, Mr. Abraham	300
Field, Ms. Hilda B.	100
Fisher, Mr. R.J.	100
Ford, Mr. John	100
Fossett, Mr. Ralph	300
Freeman, Mrs. M. Joan	200
French, Ms. Thelma	100
Freybe, Mr. Ulrich C.H.	500
Galloway, Mr. E. James	200
Gardner, Ms. Hilda	200
Germain, Ms. Shirley	1,000
Goon, Mr. Lawrence	100
Gracia, Mr. F.	100
Grant, Mr. John	750
Greer, Mr. & Mrs. Leonard	100
Grieg, Mr. John	250
Griffith-Cochrane, Ms. Joan	300
Groves, Ms. Myrtle M.	100
Grundmann, Ms. Jean	200
Gurd-Jensen, Ms. Susan	100
Hall, Mrs. Joan	200
Hardman, Mr. Gerald P.	1,500
Henderson, Mr. Gordon	200
Henry, Ms. Eva	100
Hess, Charlotte M.	100
Hobbis, Mr. Thos	200
Hoffheinz, Ms. Ethel	100
Hooker, Mr. Charles	1,000
Hooper, Ms. Joyce L.	150
Horodney, Mrs. Margaret	100
Huffman, W.R.	100
Huish, Mrs. Betty C.	100
Hull, Mr. Vance	100
Hungerford, Mrs. F. Mary	200
Hyatt, Mrs. Hester	100
Jackson, Mr. & Mrs. W.R.	100
Jacobs, Mr. Raymond A.	100
Jennings, Mr. D.	100
Johnston, Drs. W. & R.	100
Jukes, Mr. Andrew J.	250
Kacan, Mr. Sandy	1,000
Kelch, Mr. Gerd	100
Kellington, Mrs. Sheelagh	200
Kenyon, Mr. J. Michael	250
Keogh, Dr. & Mrs. J.	100
Khnana, Mrs. Debbie	100
Killin, Mr. A.F.	100
King, Mrs. Catherine	100
King, Ms. Ella G.	485
Klassen, Ms. Marie	100
Kustan, Dr. Edward H.	100
Laudisio & Family, Mr. A.	100
Lawson, Frances	132

Lazenby, Mrs. Annie Gladys	250
Lee, Mr. & Mrs. James	125
Lee, Mr. Duncan W.	250
Lewis, Mr. & Mrs. Glen E.	100
Lichtenfeld, Mr. Joseph	100
MacDonald, Ms. Helen R.	100
MacDougall, H.J.B.	100
Machin, Ms. Celia	200
MacIntosh, Mr. Robert	100
Mackay, Miss Elizabeth	175
Mah, Ms. T. Gail	250
Manson, Dr. A. David	100
Mapson, Marjorie	100
Marshall, Mr. J.G.	200
Maxwell, Mrs. Margaret	500
McCurdy, Ms. Diane L.	100
McKay, Mr. & Mrs. F.	100
McMahon, Mr. E. Michael	250
McMillan, Mr. Thomas	100
McTaggart, Mr. A.E.	300
Merriman, William	100
Milne, Miss Jean	100
Moffat, Margaret	100
Mohrman, Miss Freda	100
Mold, Mrs. Eileen E.	100
Molson, Mrs. R.J.	200
Montgomery, Mr. Elmer	100
Moody, Ms. Joanne L.	100
Moody, Ms. Betty	100
Moore, Ms. Victoria M.	1,000
Morrison, H. Frances	100
Morton, Mr. Bruce	100
Murray, Mr. Donald	150
Mutter, Mr. R.	100
Myoshi, Arlene	100
McKinnon, Mr. J.	100
Nash, Charlie & Mary	100
Nataros, Dr. H.S.	100
Neilson, Mr. & Mrs. James	100
Nip, Esther	100
Paisley, J.W.	120
Parsons, Mr. R. Brian	100
Paterson, Mr. L.	100
Pawlitza, Vera R.	400
Pedersen, Ms. Inger	1,000
Pekrul, Mrs. M.	100
Penzer, Ms. Belynda	100
Perry, Rose J.	100
Pfeifer, Mrs. Gordon	100
Phillips, Ms. Lorraine D.	100
Piercy, Mr. Clive	100
Pike, Mr. James A.	200
Pinchin, Mrs. Janet	200
Pinnell, Ms. E. Patricia	150
Randhawa, J.	100
Ranson, Irene Joyce	350
Read, Mrs. Christina M.	100
Reddy, Dr. Suseela	100
Reddy, A.R.	100
Reeder, Mr. & Mrs. Herb	1,000
Reelie, Mr. Gordon	5,000
Riley, Margaret	100
Robbins, E. Madge	100
Roedde, Ms. Madeleine	100
Rooney, Mrs. Muriel E.	500
Ross, Mrs. Iola M.	200
Royal, Marjorie I.	100
Rubenstein, Mr. Jonathan A.	100
Rummel, Mr. & Mrs. A.	100
Russell, Ms. Matilda	100
Santacroge, Mr. Peter	100
Schramm, Mr. Richard	500
Shaw, Nancy	120
Shone, Ms. Edna J.	500
Skarsgard, Dr. Lloyd	100
Skov, Mrs. Esther	500
Smelser, Ms. Jeanne	100
Smith, Mrs. Hilda	100
Smith, Harold	100
Southam, Mrs. Gordon	1,000
Southam, Mr. & Mrs. Gordon T.	250
Spink, Mr. John	200
Spry, Mr. & Mrs. J.E.	100
Stearns, Mrs. Phillis	20,000
Steele, Mr. Frank	100
Sterling, Mr. W.J.	100
Stewart, Mrs. Delia J.	500
Stewart, Mr. Oswald J.	500
Stout, Susan & Bruce	100
Stushnoff, Mr. & Mrs. Joe	200
Suddard, Mrs. Gladys	100
Sung, Miss Lily K.S.	2,000
Sutherland, Ms. Fannie	100
Swabb, Mr. William	1,500
Taggart, Judge J.D.	100
Taggart, Judge Valerie J.	500
Tateyama, Shinya	100
Tateyama, Julie	100
Taylor, Mr. James E.	100
Thompson, Ms. Miriam	100
Thorne, Ms. Vera R.	100
Thorne, Mr. Walter E.	100
Timbers, L.E.	300
Tobin, Mrs. Lillian	110
Toews, Ms. Mildred	100
Trifaux, Margaret	100
Tsui, Ms. Margret	100
Turpin, Mrs. Marion L.	100
Underhill, Mr. Richard W.	100
Uridge, Mr. Donald	100
Van Dorn, Mrs. Mary	200
Van Roggen, Ms. Jane	200
Van Tienhoven, Jessie	100
Voth, Mr. & Mrs. George	100
Walker, Mrs. Agnes	500
Walsh, Mrs. Isabel	100
Walwyn, Timothy	100
Watters, Mr. John I.	100
West, Mrs. Edith H.	4,000
Wiens, Dr. A. Thomas	200
Wildy, Mr. & Mrs. Tony	120
Wilkinson, Mrs. A.	100
Williams, Mr. Brian R.	100
Wills, Mr. Charles	500
Wing, Ms. June	250
Winskill, Ms. Aileen	2,000
Wong, Ms. Donna E.	100
Woo, Mr. Ronald	100
Wu, Thomas	100
Yen, Mrs. Sue May	100
Yip, Buck W.	100
Zorn, Mr. Joseph	100
Akrigg, C.	1,127
Hayes, P.A.	100
Jambor Family (Fund)	35,937
Grieg, Anna Ruthven (Fund)	1,045
Hogarth, Madge (Fund)	2,075
Collins, Mark & Phae (Fund)	2,000
Donations less than $100	55,786
Total	284,154

Donations designated for specific purposes:

Greater Victoria Hospital Society	1,500
RJH Employees' Community Fund	1,000
Cancer Control Unit-HEU Local 180	100
Rotary Club of Sydney	250
Anonymous	4,000
Knoll Pharmaceuticals Canada Inc.	100
United Way of the Lower Mainland	5,167
Philips Electronics Ltd.	1,000
Arthur Andersen & Company	600
Walter A. Pawluk	100
Victoria Cancer Clinic	470
E.J. Phillips Medical Ltd.	500
Provincial Chapter IODE	12,000
Rhone-Poulenc Pharma Inc.	1,000
Novopharm Ltd.	100
McGill & Orme Limited	270
L.D. Sullivan Incorporated	500
IODE Malaspina Chapter	100
L. Hamel Ltd.	250
C.J. Coady & Associates	200
Canadian Red Cross Blood Transfusion Service	200
Herbert T. Hart & Co. Ltd.	200
St. Rupert Equities Inc.	5,000
Transco Mills Ltd.	200
Blue Unicorn Soccer Team	200
Women of the Moose	200
Vancouver School of Theology	500
Order of the Eastern Star	14,459
ICI Phara	500
Royal Bride Chapter, IODE	500
Honeywell Bull	500
Seacrest Sales Ltd.	100
Dufferco Ltd. (U.S.A.)	500
Steetley Distribution Inc.	200
Olympia's Westwater Inn	1,000
Bristol Myers Pharmaceutical Group	500
Prepared Media Laboratory, Inc.	100
Becton Dickinson Canada Inc.	500
Carl Zeiss Canada Ltd.	500
Horner	500
Secret Cove Resort Ltd.	100
La Grotte Restaurant	150
Ladies Aux. Crescent Legion No. 240	150

Josco Holdings Ltd.	7,500
Chief & Petty Officers Veterans	1,200
Martlet Chapter, IODE	800
United Commercial Travellers Cl 434	545
Jurg Berchtold Enterprises Ltd.	424
C.H. Cates & Sons Ltd.	2,000
Carsen Medical & Scientific Co. Ltd.	250
U.B.C. Health Sciences Centre Hosp.	1,000
Grand Chapter of B.C. & Yukon-O.E.S.	665
Holy Order of Mans	500
Vancouver School of Theology	500
Diamond Foundation	25,000
Society for Oral Oncology	1,000
Westwood Pharmaceuticals	1,000
Order of the Eastern Star	2,000
Alcorn, Mr. Gary	150
Algard, Mrs. Annette E.	100
Anderson, Dr. George	100
Ankenman, Dr. G. John	500
Auyeung, Pui-Ying	300
Baker, Dr. Clarice A.	100
Band, Dr. Pierre R.	100
Basco, Dr. Vivien	100
Beer, Dr. Charles T.	4,000
Berry, Mrs. Lucy M.	150
Blundell, Mr. Alfred	5,000
Boyes, Dr. David A.	100
Brady, Mr. & Mrs. Robert	150
Bray, Mrs. Cynthia M.	2,000
Burns, Harvey & Marg	100
Cairns, Dr. E.M.	200
Cambon, Dr. E.	100
Caulfield, Dr. William	100
Chan, Dr. Seck	200
Chin, Ms. L. Anne	500
Cleeton, Mr. A.J.	100
Coggin, Ms. Mary	2,000
Cohen, Mr. Joseph H.	7,500
Connors, Dr. Joseph	300
Coppin, Dr. C.M.L.	500
Coulter, Mr. Albert N.	1,000
Cox, Dr. Leonard	200
Coy, Dr. Peter	200
Crawford, Dr. Glen	100
Cupp, Mr. Christopher R.	100
Curry, Ivan & Jean	100
Davidson, Ms. Gladys	500
Dixon, Dr. K.W.	100
Dmytryshyn, Mrs. Joan	100
Dukelow, Dr. James	100
Eaves, Dr. Allen	100
Edwards, Mr. Harley	2,000
Emmons, Ms. Helen J.	100
Evani, Dr. S.V.	500
Evans, Dr. Adele M.	850
Family, the Signorello	100
Fetterly, Mr. John	200
Fewster, Ms. Lilian F.	500
Flores, Dr. A.A.	175
Flynn, Ms. Susan	100
Forsyth, Mr. William	300
Fritz, Dr. Bradley A.	250
Gerrard, Mr. John	100
Gibbins, Mr. John	137
Goldenberg, Dr. Larry	100
Gowd, Dr. G.B.	100
Grant, Jean E.	200
Hague, Mrs. P.M.	100
Halley, Mr. James M.	100
Hanson, Mrs. Anne T.	200
Hanson, Mr. Fred G.	200
Harris, Miss Viola T.	1,000
Haveling, Mr. Wayne	500
Hawkins, Mrs. John	100
Haynes, Mr. William A.	1,000
Hedges, Ms. Doreen	100
Helgason, Dr. Robert E.	100
Hill, Dr. Robert	500
Irving, Ms. Mary J.	100
Jackson, Dr. Stewart	100
Jackson, Dr. Gary C.	150
Jamieson, J.	250
Johnstone, Mr. Trevor	100
Jones, Dr. Norman H.	100
Kallio, Ms. Jean	100
Keatinge, Mr. G.A.	2,000
Kelly, Mr. Frederick B.	100
Kent, Dr. Henry P.	500
Kim Sing, Dr. Charmaine	100
Kinloch, Mr. Henry	500
Klaassen, Dr. David	200
Klishan, Ms. Rita	200
Knowling, Dr. Meg	100
Kostashuk, Dr. Ed	500
Lam, Dr. Stephen	100
Layada, Mr. A.	200
Le Rose, Mr. Geno	100
Leach, Mr. Derek	200
Lerose, Geno	100
Lichtenfeld, Mr. J.	200
Linton, L.A.	300
Locke, Mr. Harold	100
Lum, Ms. Lilian	100
MacKay, Dr. Colin B.	325
Mallen, Dr. Peter	100
Massullo, Mrs. Florida	100
McCoy, Mrs. W.A.	200
McDonald, Ms. Ann N.	350
McDonald, Mr. W. Kyle	250
McGregor, Ms. Janet M.	100
McGregor, Dr. Gregor	100
Messere, Ms. Dianne	100
Michelmore, Mrs. Irene M.	500
Miller, Ms. Violet	1,000
Morrison, Dr. M.D.	100
Mouat, Ms. Isabella	200
Mueller, Dr. H.A.	100
Murphy, Dr. Kevin C.	550
Murray, Dr. Nevin	100
McAllister, Mr. & Mrs. Robert	100
McCollin-Moore, Rev. E.	500
Nelson, Mrs. Sheila M.	500
Newby, Mr. W. Maxwell	100
Newcomb, Flora M.	100
Pepper, Dr. Verne	100
Pettapiece, Dr. H. Graham	100
Plenderleith, Dr. Ian	150
Preto, Ms. Christine	200
Pringle, Dr. Donald	100
Quintrell, R.N.	100
Richmond, Dr. & Mrs. Allister	100
Robins, Dr. Edward	100
Rolls, Ms. Bernice	100
Romano, Mr. Mario	100
Royle Inc., Dr. N. Derek	100
Sawyer, Mr. & Mrs. Lloyd	200
Schwerdt, Mrs. Jean	200
Seifner, Mr. Paul	1,000
Sigal, Ms. Elana	100
Simpson, Dr. Charles	100
Smith, Ms. Nora Jane	100
Smith, Mrs. Yvonne L.	100
Snyder, Mrs. Jean N.	1,000
Soares, Mrs. Wellyn	500
Soares, Ms. Wellyn	500
Spence, Ms. Lindsay	100
Stevenson-Moore, Dr. Peter	100
Stoddart, Mr. John	100
Such, Mr. Lionel	100
Surine, Ms. F.H.	125
Sutter, Dr. Mary Alice	100
Swanson, Dr. Alva E.	100
Taylor, Ms. Betty	500
Tobias, Ms. Donna	100
Trudeau, Ms. Shirley	200
Twiddy, Mrs. Gwen	750
Van Der Vliet, Ms. Helen	1,000
Van Slatte, Mr. Philip	500
Vosburg Ford, Janet	1,000
Walton, Mr. Kenneth	1,000
Warkentin, Mr. & Mrs. Peter	100
Wilford, John & Agath	100
Wilkinson, Mrs. Anne M.	100
Wilson, Dr. I.	100
Woo, Dr. Young Chi	200
Woodham, Dr. Jeremy D.	100
Wosk, Mr. & Mrs. H.	100
Yip, Dr. Suzanne	200
Yuen, Dr. Kenneth	100
Zimmerman, Mrs. Betty	200
Telephone Employees Community Fund	11,150
Order of the Eastern Star	2,000
Donations Under $100	24,601
Total	198,864
Total Donations	$483,018

Bequests from the Estate of the Late:

Bakrud, Lester	$ 1,000
Bartlett, Katherine I.	29,576
Brown, Marion C.	84,519
Dickson, Evie	14,300
Gegolich, Sonia	4,156
Gordon, Sheila Diana	57,620
Graham-Marr, Anita G.	10,875
Hector, Charles F.	1,765
Hellum, Ib Christen	100
Hendry, Margaret	5,000
Irwin, Maxine D.	3,594
Johnston, Alexander M.	5,000
Jones, Elizabeth Owen	112,347
Killam, Estella May	20,000
Little, Eleanor Graham	764
Lucas, Thomas	500
McCallum, Stuart	1,000
McGirr, Emma Amy	1,500
McGirr, Edward Charles	1,500
McPherson, Charles Thomas	5,000
Malley, Joseph Smith	1,000
Markin, Valentina	5,000
Nicholson, Charlotte J.A.	5,000
Paradis, Antoinette B.	2,387
Risse, Alice Maude	123,415
Rounsefell (Memorial Fund)	17,141
Scott, M.	936
Siegel, Eleanor Eva	94,570
Squires, Myrtle	250
Stensones, Maria Genova	10,000
Sutcliffe, John P.	1,000
Tillman, Estelle	1,236
Tweedie, Edith (Memorial Fund)	2,208
Valk, Martha T.	500
Vince, Elizabeth Eva	67,343
Wallbridge, Grace E.	2,000
Wickett, Edna Alice	46,855
Wilbee, Phyllis M.	11,345
Wilkerson, Katherine	2,496
	$754,798

Bequests designated for specific purposes:

From the estate of the late:

Carlin, Connie Bessie	$ 1,000
Coe, Florence	53,053
Morgan, Violet	10,000
Sweet, Jessie L.W.	1,530
Royal Trust (for the Lavender Memorial Trust)	40,000
	105,583
Total Bequests	860,381
Total Donations & Bequests	$1,343,399